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I

MANAGEMENT OF CARDIAC STANDSTILL DURING OTOLARYNGOLOGIC SURGERY

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NEW ORLEANS, LA.

Reliable statistics[1] reveal that death during general anesthesia still remains a definite possibility in spite of development of newer anesthetic agents and improvement in both anesthetic and operative techniques. Therefore, since tonsillectomy continues to be the most frequently performed surgical procedure in the United States,[2] otolaryngologists should be familiar with proven methods of combatting impending death under general anesthesia. This is particularly true because in many instances nurse anesthetists are used, and when emergencies occur the otolaryngologist is expected to assume leadership in carrying out resuscitative measures.

Impending death from cardiac or respiratory arrest is the foremost operative emergency. Time is of the essence if resuscitative measures are to be successful, hence a predetermined plan of attack based on sound physiological principles should be instituted promptly.

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It is the purpose of this presentation to review the physiologic basis of modern resuscitative methods and to make recommendations as to resuscitative medication and equipment that should be readily available whenever otolaryngologic surgery is done under general anesthesia. Also, we shall offer suggestions as to a procedure of therapy to be used in these emergencies. Finally, we shall review a case of cardiac arrest following tonsillectomy under general anesthesia.

ETIOLOGY

Although the cause of cardiac arrest is often difficult to determine, some of the etiological factors are understood. Certain anesthetic agents, e.g., cyclopropane, chloroform, and ethyl chloride, sensitize the heart to epinephrine.[3] Hypoxia will also sensitize the heart and the carotid sinus and increase the epinephrine content of the circulating blood. Intravenous barbiturates and cyclopropane have a parasympathetic or inhibitory effect on heart action.[4] The mechanism of the vago-vagal reflex is well established.[5] Heart activity may be slowed or stopped by too deep anesthesia of any type. The individual heart may have a low inherent tolerance to a particular anesthetic agent; this may be found in an apparently healthy heart or in a heart whose myocardium has been affected by acute or chronic disease. Finally, there are those cases of cardiac standstill secondary to peripheral vasomotor collapse.

PATHOLOGIC PHYSIOLOGY

A rational approach to the management of cardiac arrest demands that two fundamental types of death be differentiated.[6]

The first type is general death, sometimes known as unmanifested or latent life; in this condition circulation and respiration have ceased but the organs are still living and resuscitation is possible though complete recovery of function may not always be obtained. If the patient is to survive, resuscitative measures must be initiated as early as possible during this period. Further, it should be emphasized that the earlier these measures are instituted the better are the chances for complete recovery.

The other type is elemental death; in this condition protoplasmic disintegration and tissue death are brought about by enzymatic action. These changes are irreversible and resuscitative measures will not restore function. The rate of progression of elemental death is not the same in all organs. Unfortunately, the most rapid rate of development occurs in the brain where the time element for some portions is felt not to exceed 3½ minutes.[7] Adequate resuscitative

measures begun after this time has elapsed may result in recovery, but in the majority of instances there will be some permanent change in the psychic behavior of the patient.

Since resuscitative efforts should be directed not only toward saving life but also toward preservation of an undisturbed psyche, a review of a few pertinent facts concerning circulation in the brain and the physiology of the arrested heart would seem to be in order.

Experiments have shown that the basal blood requirement of the brain at rest is about 1400 cc per minute provided the blood is normally oxygenated.[8] This represents one-third of the ventricular output although the brain represents only two percent of the body weight. If central nervous system circulation is not adequate the probable order of neuronal vulnerability, determined in patients who had survived varying periods of cardiac arrest, is as follows: the smaller pyramidal cells of the medulla, retina, and spinal cord, and cells of the spinal root ganglia.[9] It becomes obvious then that when these crises occur cerebral circulation of oxygenated blood should be maintained by whatever means possible; these include lowering the head of the operating table, artificial respiration, and most important, cardiac massage.

A knowledge of certain practical aspects of the physiology of the arrested heart is essential if adequate resuscitative methods are to be used. It is known, for example, that, in some instances, even though peripheral circulation cannot be detected, some heart action may still be present.[10] When general death has ensued, i.e., when heart action has ceased, the individual muscle bundles of the myocardium apparently retain the ability to react to stimuli. Should any portion of the musculature become temporarily more irritable than the sinus node, stimulation in this area may initiate cardiac contration.[11] This is the basis for the efficacy of needling the heart in some cases and of cardiac massage in others. Of practical value, too, is the fact that laboratory experiments[12] have demonstrated that the auricles are more sensitive to mechanical stimulation than are the ventricles. Further, ventricular stimulation may lead to ventricular fibrillation and death. This proportionately lower sensitivity of the ventricles may be a fortunate circumstance since if an ectopic focus of extrasystoles occurs in the auricles, the ventricular response may be normal except for premature contractions, the bundle tissue having filtered out many of the stimuli. The sensitivity of the ventricle may be further lowered and the possibility of an ectopic ventricular focus thereby averted to some extent by the use of procaine either in the cavity of the heart or topically. It would appear,

therefore, that any resuscitative stimulus in the form of puncture or massage should best be directed to the base of the heart rather than to the apex.

In the use of artificial respiration advantage may be taken of certain facts known about the physiology of the disturbed respiratory system in these emergencies. Artificial respiration with 100 per cent oxygen rather than with an oxygen-carbon dioxide mixture should be used due to the fact that once the respiratory center is depressed beyond a certain point carbon dioxide acts as a depressant rather than a stimulant. In addition a "suck and blow" type of artificial respiration would seem preferable to any other type if experimental findings are valid.[14] The superiority stems from the fact that although both inflation and deflation reflexes have been demonstrated, none are known to exist for mere passive deflation or expiration such as is accomplished with the regular gas machine. On the other hand, suction applied to the trachea and bronchi sets up a more potent stimulus to respiration than does inflation.[15] This potent stimulus lengthens the critical limit for recovery from respiratory arrest by about two minutes over that with manual artificial respiration, whether or not the latter is combined with oxygen-carbon dioxide mixtures.[16] Because of the time factor "suck and blow" respiration should be instituted as quickly as possible. Two final remarks concerning artificial respiration in these crises would seem to be noteworthy. The first is that in addition to its ventilatory function artificial respiration may aid in the circulation of the blood.[17] The other is that respiratory recovery often lags behind cardiac recovery, and artificial respiration may have to be continued for a prolonged period of time.

THERAPEUTIC OBJECTIVES

From the foregoing it is evidence that therapy in cardiac standstill should be started without delay as soon as the diagnosis is made and should consist of maintenance of circulation and oxygenation of the blood while efforts are made to stimulate the heart and respiratory system to resume their normal activity. An apparently successful outcome of the episode should not lull the physician into a sense of false security for it is well known that these patients may die many days postoperatively; therefore, the necessity for remote aftercare and observation is implied.

CARDIAC RESUSCITATIVE MEASURES

Three types of cardiac resuscitative measures may be used either alone or in combination. These are:

1. Intravenous resuscitation.
2. Intracardiac injection.
3. Cardiac massage.

Intravenous Resuscitation. Almost all cases of cardiac arrest are reported as occurring suddenly and without previous warning. Yet, most anesthetists agree that if the patient's pulse is checked closely enough certain signs of impending disaster can be detected. These include an initial tachycardia followed by a gradual slowing of the rate, short periods of arrest, dropped beats, and extrasystoles. If these prodromal signs are recognized and treatment promptly instituted, cardiac arrest may be avoided.

Procaine is the drug of choice for treatment of these cardiac irregularities. As mentioned previously it elevates the sensitivity threshold of the ventricle and thereby decreases the possibility of ectopic foci being established. The dosage of procaine for intravenous use may be as much as 100 milligrams used either in a 1 per cent (10 milligrams per cubic centimeter) or 2 per cent (20 milligrams per cubic centimeter) solution. It should be rapidly injected into the anticubital vein and prepartions for intracardiac injection made if there is no response within forty-five seconds. The tendency for procaine to stimulate the central nervous system is counteracted by the general anesthetic being used.

The efficacy of procaine in these cases has been demonstrated by Burstein.[18] He reported fourteen cases of acute cardiac dysfunction arising during cardiac surgery in which intravenous procaine seemingly restored normal rhythm. Furthermore, he has shown that even when ventricular fibrillation has set in, intracardiac injection of procaine may result in a return to normal sinus rhythm.

Intracardiac Injection. Confusion seems to exist regarding just what is meant by the term "intracardiac injection." At times it has been applied to injection into the myocardium while at others it has been used to designate injection into the lumen of the heart. Hyman[11] indicates that injections into the myocardium, particularly that of the auricle, are the most effective. However, we feel that it is safer for those inexperienced in cardiac needling to make the injections into the lumen when the heart is arrested; if slight activity is detected by the needle, the lumen should not be entered.

The increased emphasis placed on the value of cardiac massage, while certainly correct, has unfortunately served to overshadow the value of intracardiac injection. Though the procedure is admittedly

often ineffective it is interesting to note that a review of the literature in 1945 revealed 33 per cent of the cases of cardiac massage to be successful[19] whereas up to 1921 success had been achieved in 26 per cent of the injections done.[20] Bailey[1] incorporates intracardiac injection into his resuscitative procedure by performing it while preparation is being made for massage. Lahey and Eversole[10] advocate that the cardiac needle be inserted into the heart as soon as the diagnoisis of asystol is made. Their reasons are twofold: 1) the presence of a faint heartbeat, not sufficiently strong to produce a peripheral pulse, may be detected by movement of the needle, and 2) the pricking of the heart may initiate cardiac activity if none is present.

Many solutions have been used for intracardiac injection, but it has not been definitely determined whether or not they are pharmacologically effective in initiating cardiac activity following arrest. It is possible that a favorable response may be on the basis of the stimulus from injection. Epinephrine, for example, continues to be the most frequently used substance and recoveries are reported following its use despite the fact that it has been shown to be harmful in some cases.[21]

The approach used in intracardiac injection depends on whether one desires to enter the auricle or the ventricle. Based on what has been said previously, auricular puncture would appear to be most logical. However, in either case the procedure is not difficult. A 19 gauge needle, four and one-half inches long, with an attached 5 cc syring containing 0.25 cc of 1:1000 epinephrine in 4.75 cc of 1 per cent procaine is used. The needle should be of this length because in wide chested individuals the right auricle may be as much as four inches from the anterior surface of the sternum. In children up to twelve years of age it will be found within two inches of the anterior surface of the sternum, while in the average adult this figure is increased to about three and one-half inches. The ventricle is closer to the chest wall.

If the auricle is to be entered the needle is inserted through the third right interspace at the upper rim of the fourth rib, close to the sternal border as possible. It is directed slightly medialward and posteriorly until blood can be withdrawn into the syringe as evidence that the tip of the needle is in the lumen of the auricle. At this level the first structure encountered is the auricle; the great vessels are located several inches above and below.

When ventricular injection is to be done the needle is inserted into the fourth left interspace at the upper rim of the fifth rib, close

to the sternal border. It is directed slightly medially and posteriorly to enter the right ventricle.

Intracardiac injection is not without danger, but the gravity of the situation seems sufficient to warrant its use. It is well known, for instance, that if the myocardial structure is hyperirritable during standstill, the slightest cardiac stimulation of any type may cause fatal fibrillation. Then, too, cardiac tamponade may ensue as a result of leakage of blood into the perecardial sac; this is more likely to occur if multiple punctures are made. To forestall this latter eventuality it is recommended that when cardiac activity does not immediately follow injection the needle be left in situ for 30 seconds at the end of which time a second injection may be made. Should any evidence of cardiac activity be obtained the needle is slightly withdrawn until the course of development of this reactivation can be determined. By this maneuver the possibility that the needle may act as a noxious stimulus is avoided.

Cardiac Massage. This is the most important single procedure in the treatment of cardiac arrest; all others are merely stop-gag measures used until massage can be started. Of the known resuscitative measures it offers the best chance for recovery provided the blood is well oxygenated and the procedure is initiated early. Properly performed, massage accomplishes three things: 1) Mechanically empties the engorged chambers, 2) mechanically stimulates the myocardium, and 3) creates an artificial circulation to transport oxygen to the hypoxic tissues.

Three approaches to the heart are available for the purpose of massage: the transperitoneal subdiaphragmatic, the transperitoneal transdiaphragmatic, and the transthoracic. The latter is undoubtedly preferable, but under ordinary circumstances the average otolaryngologist will find either of the first two mentioned approaches more feasible.

In the transperitoneal subdiaphragmatic approach a midline incision is made in the epigastrium and the right hand inserted into the abdominal cavity between the superior aspect of the liver and the diaphragm. The heart is located and gentle intermittent compression started while simultaneous counterpressure is being made with the left hand pressed against the lower costal margins anteriorly. The advantage of this method lies in the speed with which it can be performed; the disadvantage is the fact that there is incomplete emptying of the non-apical portion of the heart. In the transperitoneal transdiaphragmatic approach recommended by Nicholson[23] an incision several centimeters in length is made in the diaphragm be-

hind the sternum and the thumb of the right hand inserted through this opening. The heart is then compressed between the thumb and the fingers beneath the diaphragm. This method has the advantage of allowing better massage though it is somewhat more time consuming. In either case there will be no bleeding from the wound margins since there is no circulation. As soon as caridac activity has been revived the abdominal incision should be closed with through and through sutures. This type of suturing is indicated because if massage has to be reinstituted the incision can be opened with a minimum of difficulty. The buttonhole incision in the diaphragm need not be sutured.

As mentioned previously the massage should be gentle for otherwise the heart may be seriously traumatized. Gunn[24] advises that the compression be gradual and the relaxation abrupt and that a rate of about 40 per minute be maintained. This lower than normal rate of compression is recommended in order that the ventricles may be allowed to fill completely and also because it approximates the rate at which cardiac activity is resumed. At regular short intervals the massage should be interrupted in order to allow spontaneous beats to develop. Additional drug therapy may be used simultaneously with the cardiac massage.

BASIS FOR SUCCESSFUL RESUSCITATION

Sufficient evidence has accumulated to indicate that a surprisingly high percentage of complete recoveries can be obtained in these cases providing:

1. The operating team is well-trained in a predetermined plan of attack based on sound physiological principles,

2. The proper emergency equipment and medications are immediately available, and

3. Resuscitative measures are begun early.

THE OPERATING TEAM IN RESUSCITATION

A consideration of the operating team personnel must necessarily begin with the anesthetist as he should be the first to recognize and report the presence or suspicion of cardiac standstill. Alertness and quickness of action is required. Endotracheal intubation should be immediately performed and some type of artificial respiration with 100 per cent oxygen instituted. Therefore, the anesthetist should be well accomplished in the techniques of direct laryngoscopy and endotracheal intubation. To some this may seem surprisingly fundamental, yet it is widely known that a goodly proportion of the

persons giving anesthetics for tonsillectomy are not proficient in these two procedures. If the otolaryngologist has to take over and perform the intubation precious time will be lost, time during which he should be making efforts to revive the heart. Moreover, the anesthetist should have a battery-handle laryngoscope, an endotracheal tube of proper size, and suction catheters laid out on a nearby table top so that they may be available for immediate use. If a "suck and blow" respirator is available he should be familiar with its location and operation so that it may be employed without delay.

Concerning the otolaryngologist in the operating team, a quotation from Fauteux[25] is very apropos: "Surgeons should be trained in cardiac resuscitation techniques, and should not wait for emergencies at the operating room to gain experience." He should realize that the main object is to start cardiac massage as soon as possible. There should be no time wasted with any lesser measures that would delay the accomplishment of this objective. In addition, the surgeon should satisfy himself that his anesthetist is capable of coping with the situation and that the operating room he generally uses is stocked with adequate equipment and medications. In these apalling emergencies foresight is much better than hindsight, and it is a consolation to know when one loses a patient while undergoing one of these so-called "relatively safe minor procedures" that everything possible in the light of our present knowledge has been done to save him.

All that can be asked of the assistants and circulating nurses is that they be familiar with the location in the operating room of various resiscitative equipment and medication and that they carry out the surgeon's orders quickly, accurately, and with a minimum of confusion.

PLAN OF THERAPY

Treatment of cardiac standstill consists of three distinct phases:

1. Preventative therapy
2. Resuscitative therapy
3. Aftercare

Preventative Therapy. The aim of this phase of therapy is to make the patient the best possible operative and anesthetic risk. Towards this end he should receive preoperatively a thorough physical examination, any anemia present should be corrected, existing infection eradicated, and the nutritional state improved if necessary. Because children should not be regarded as merely "little adults," their

management requires specialized knowledge, and the service of a pediatrician is indispensible.

An extremely important, though too frequently neglected aspect of preventative therapy, is the proper psychologic preparation of the patient. That psychic trauma does occur in many cases must be obvious to anyone who has witnessed a terrified, struggling, and screaming child fighting the anesthetist before and during induction. Levy,[26] in an excellent presentation, has demonstrated that emotional sequelae may result from such psychic trauma. In addition it should be remembered that deaths from sheer fright have occurred in the operating room.

Effective psychologic prophylaxis requires an understanding of the average child's reaction to the awareness that he is to undergo anesthesia and an operation. To him it represents a venture into the unknown away from the familiar home and the protecting parents—the main sources of his security. He will be handled by strange people in strange surroundings. Furthermore, he will experience unfamiliar and unpleasant odors, be placed in the usual stark white operating room surrounded by weird instruments, and be ministered unto by people in white, some of whom hover over him and some of whom move about in the distance. To these may be added the fear of possible pain and of being forcibly put to sleep by having a mask of some type placed over his face. These experiences produce mounting excitement, a spiraling metabolic rate, increased production of epinephrine, and many other changes. Under these conditions physiologic disturbances are apt to occur which may eventually affect the cardiac musculature and predispose to arrest.

To minimize the psychic trauma of operation certain steps may be taken. The child should be made to feel that it is the necessary thing to do and that many other children have had the same operation performed. A simple, brief explanation of the operation should be given and this repeated as many times as necessary; the feeling that a thing is explained, even if the explanation is inaccurate, serves to relieve tension. The person the child is closest to should accompany him to the hospital and administer to him during the immediate preoperative period until the premedication given has had its effect. Ideally, the child should be spared the experience of seeing instruments, the operating room and its unusually clad personnel, and being wheeled through the unfamiliar hospital corridors and riding up the elevator. He should be asleep from the time he leaves his room until he returns.

There is still much debate concerning the advisability of premedication in children. Many otolaryngologists and some anesthetists

oppose its use. Yet those doing pediatric surgery of other types use it routinely and have a sound physiologic basis for so doing. It would appear that the difficulty experienced with premedication in the past resulted from a lack of knowledge of their proper dosage rather than from the agents themselves. All prescribing these drugs should familiarize themselves with the proper dosages as advocated by authorities on the subject.

Of the premedicaments, the belladonna and barbiturate derivatives have the widest range of usefulness. The belladonna group is the most important because its members depress the vagus endings in the pharyngo-tracheo-bronchial area and thereby lessen the possibility of difficulty being encountered as a result of the vago-vagal reflex. The barbiturates act by allaying the emotional tension of the patient and thereby preventing an increase in the rate of metabolism and epinephrine production and release. In addition they cause the central nervous system to become more receptive to the action of general anesthesia. It should be emphasized that the purpose of premedication is defeated if sufficient time is not allowed for the drugs to have their full pharmacologic effect. Furthermore, anesthesia may be made unnecessarily difficult and dangerous if this point of full pharmacologic effect does not arrive until the patient is anesthetized; when this occurs the patient may, for no supposed reason, go to a surprisingly deep stage of anesthesia and thus be exposed to undesirable consequences.

As we have previously mentioned certain cardiac irregularities occurring during the course of general anesthesia are often prodromal signs of cardiac standstill. Treatment of these irrigularities by the intravenous administration of 50 to 100 mg of procaine in a 1 or 2 per cent solution may correctly be included as a preventative measure.

Resuscitative Therapy. Once actual cardiac standstill has occurred a planned method of attack should be instituted immediately because cardiac massage must be begun before three and one-half minutes have elapsed.

The anesthetist should as soon as possible accomplish the following:

1. Begin artificial respiration with 100 per cent oxygen, preferably through an endotracheal tube.
2. Clear the airway of any accumulated secretions.
3. Lower the head of the operating table.

4. See that there is no pressure in the region of the carotid sinuses. This will immediately relieve the condition if it is due to a carotid sinus reflex.

5. Place an opened ampoule of amyl nitrite in the closed artificial respiration system. If asystole is due to "operative faint" the powerful stimulating effect of amyl nitrate on the myocardium will quickly correct this condition.

6. Call for a "suck and blow" type of respirator and begin using it as soon as it is available.

The surgeon should spring into action as soon as the diagnosis is made. In general the following is the procedure which should be used:

1. Order the assistant and scrub nurse to make preparations to institute cardiac massage.

2. While this is being done forcibly thump the precardial area with the fingers several times in an attempt to institute cardiac activity.

3. As soon as the materials are available inject 0.25 cc of 1:1000 epinephrine in 4.75 cc of 1 per cent procaine into the lumen of the right auricle. If cardiac activity does not immediately follow injection, the needle should be left in situ for thirty seconds at the end of which time a second injection may be made. However, should any evidence of cardiac activity be obtained the needle is slightly withdrawn until the course of development of their reactivation can be determined. To either of the injections atropine grains 1/200 may be added. It must be emphasized that cardiac injection should be done only if time permits; otherwise this step is omitted and all efforts directed to early institution of cardiac massage.

4. By this time the abdomen should have been prepared by the assistant. A median or left paramedian incision is made and massage begun via either the transdiaphragmatic or subdiaphragmatic route. The compression should be gentle and gradual and the relaxation abrupt. A rate of between 16 and 40 per minute is maintained. An occasional additional intracardiac injection may be tried if desired. At regular intervals massage is best interrupted in order to allow spontaneous beats to occur. Should any sign of activity appear massage is discontinued. It is difficult to say how long massage should be continued in the absence of activity. Generally speaking, the shorter the period of massage the better the prognosis. In our opinion it should be continued for at least one hour if the other phases of therapy have been adequate.

5. Once cardiac activity has been re-established the rhythm is usually regular because of the procaine present in the circulation. The abdomen is then closed with through and through sutures.

Supportive measures are then instituted. Oxygen is continued until respiratory activity is normal. The airway is kept patent. Plasma, blood, or 5 per cent glucose in distilled water is administered intravenously; saline should not be used to forestall edema and possible acidosis. Small doses of a pitressin-ephedrine mixture are given whenever the systolic blood pressure falls below 90 mm mercury; this mixture affords good blood pressure maintenance while not interfering with coronary artery function. Body heat is maintained with heating pads or hot water bottles. Penicillin therapy is instituted as soon as possible.

Aftercare. Vigilance is not relaxed after the patient has been returned to his room. Oxygen should be immediately available. Antibiotics are continued. A cardiologist, neurologist, and pediatrician should check the patient frequently. Electrocardiograms and roentgen examination of the chest are done at regular intervals. A close check is kept on the pulse and temperature. Large doses of the B-Complex vitamins are indicated. If pericardial effusion occurs, the fluid should be removed promptly. Intravenous procaine is given in the event that cardiac irregularities make their appearance. The patient should remain in bed for at least two weeks after which a gradual increase in activity may be permitted.

NECESSARY EQUIPMENT AND DRUGS

It is extremely important that all the equipment and drugs needed in a resuscitative plan be readily aavilable, preferably in the operating room. Furthermore, any mechanical equipment should be in working order.

A "suck and blow" type of respirator should be available for instant use and its operability checked at frequent intervals. In addition there should be at close hand a battery-handle laryngoscope, a mouth gag, a selection of endotracheal tubes of various sizes, an endotracheal tube introducer, and also a metal or hardrubber airway. It has been recommended that each operating suite have a direct reporting electrocardiograph machine.

We suggest that the indicated drugs and sterile surgical supplies be kept in a distinctly marked container whose location in the operating room is never changed. All operating room personnel should be familiar with the nature and location of these containers

frequently checked for completeness and the surgical supplies resterilized at regular intervals. This container is sealed with cellophrane tape or adhesive and the seal never broken except to meet the emergency of cardiac standstill. The contents of these containers are as follows:

1. An assortment of 3, 5, and 10 cc syringes.

2. A number of sterile 19 gauge needles, each of which should be at least four and one-half inches long.

3. A number of ampoules of the following solutions:

   1 per cent procaine
   Pitressin (20 units)
   Ephedrine sulfate (grs 3/4)
   Atropine sulfate (grs 1/150)
   Adrenaline chloride (1-1000)

4. Appropriate suture material

5. A sterile surgical pack containing:

   Scalpels
   Scissors
   Hemostats
   Thumb forceps
   An assortment of needles for closure
   Several sterile medicine glasses for solutions
   Towels for drapes

CASE REPORT

S. M. B., a 21 month old white female, was first seen on Sept. 25, 1950. The mother gave the history that the child had been subject to frequent attacks of sore throat accompanied by middle ear infections since the age of one month. There was a history of enlarged thymus which had responded to roentgen irradiation. Examination of the ears, nose, and throat revealed retracted, dull tympanic membranes bilaterally, pale allergic-type nasal mucosa, chronically inflamed hypertrophic tonsils, and hyperplasia of the other oropharyngeal lymphoid elements. Tonsillectomy and adenoidectomy were recommended and this was concurred in by the pediatrician who handled the child. The remainder of the physical and laboratory examination was negative. Accordingly, the child was prepared with a routine calcium-ascorbic acid regime preoperatively.

On Oct. 3, 1950, tonsillectomy and adenoidectomy were done. No preoperative medication was given: this was contrary to our usual routine. The anesthetic induction was begun at 9:35 A. M. and was uneventful. At first a mixture of ethylene and oxygen was used, and shortly thereafter this was changed to a mixture of 300 cc cyclopropane to 1100 cc oxygen and this continued until the patient was quiet. At this time the anesthetic agent was changed to ether by insufflation.

Seven minutes after the beginning of induction, at 9:42 A. M., the Davis-Crowe mouth gag was inserted and surgery begun. An adenoidectomy was performed with a reverse-curve La Force adenotome. The tonsils were then dissected free and removed with a wire snare. This was completed by 9:56 A. M. and at this time it was noted that the color of the blood was very dark. Following the removal of a small amount of thick, blood-free mucous by tracheobronchial aspiration the color of the blood became normal once again. To accomplish this procedure did not take more than one and one-half minutes. The color of the blood became normal almost immediately. Two sutures were then taken in the right tonsillar fossa to control hemorrhage. As the second suture was being inserted the gag reflex became hyperactive; anesthesia was not deepened, however, because the accessibility of the bleeding point was such that suturing could be accomplished in spite of the gagging. When hemorrhage was satisfactorily controlled, the surgeon removed the mouth gag, and the patient was turned on her side with her left leg flexed on the abdomen. Within a minute thereafter, cyanosis appeared and a diagnosis of cardiac standstill was made. An endotracheal tube was inserted, the head of the table lowered, and artificial respiration with 100 per cent oxygen started. Intracardiac injection of an adrenaline-procaine mixture was done while preparations for cardiac message were being made. Approximately three minutes later, about 10:45 A. M. cardiac massage was started via a transperitonel subdiaphragmatic approach. At intervals further intracardiac injections of the adrenaline-procaine mixture and of pitressin-ephedrine solution were done. During this time an infusion of 5 per cent glucose in distilled water was begun and artificial respiration continued. The color of the patient remained satisfactory.

Cardiac activity was resumed at 11:00 A. M., fifty-five minutes after massage had been started. The rhythm was normal, the pulse regular, and blood pressure was 105/80. The abdominal incision was closed and "suck and blow" respiration started. At intervals pressor drugs were administered. For the next two hours and twenty-five minutes the heart activity continued as described but the patient made only occasional gasping inspiratory efforts. At 1:25 P. M. cardiac standstill occurred once again. The abdominal incision was reopened and massage reinstituted. This was continued for another half hour, but all further efforts to revive the patient were of no avail.

SUMMARY

1. Because cardiac standstill continues to be an ever-present danger during general anesthesia, otolaryngologists should be able to institute some predetermined plan of treatment based on sound physiological principles as soon as the diagnosis is made.

2. Resuscitative efforts should be directed not only towards saving life but also toward preservation of an undisturbed psyche. Statistics reveal that these two objectives can be attained in about one-third of the cases when treatment is adequate.

3. Adequate therapy consists of maintenance of circulation and oxygenation of the blood while efforts are made to stimulate the heart and respiratory system to resume their normal activity. Another important requirement is that an artificial circulation be established within three and one-half minutes after standstill has begun.

4. Three types of cardiac resuscitative measures are discussed. Cardiac massage is by far the most important and effective of these.

5. A suggested plan of therapy to be used when cardiac standstill occurs and a list of equipment and drugs necessary to deal with these emergencies are presented.

6. A case of cardiac standstill occurring following tonsillectomy under general anesthesia is reported.

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II

LYE BURNS OF THE ESOPHAGUS

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Lye burns of the esophagus have been occurring with greater or less frequency ever since man first discovered caustic alkali during the time of Pliny.[1] The use of caustic alkali in the home manufacture of soap increased the incidence tremendously as did the use of lye, of which it is the chief component, as a cleansing agent. The cheapness and ease of purchase of soap has made unnecessary its home manufacture in this country, and so the incidence from this source is practically nil. However, the use of lye solutions to cleanse unstained wooden floors is a common practice among the negroes in the South. Containers of the solution of lye are frequently left on the floor and are readily accessible to unsuspecting children. This accounts for the high incidence among children of the colored race. The active ingredient in lye, drano and other similar cleansing agents is sodium hydroxide. Caustic alkali and sodium hydroxide are synonymous terms.

Many problems have been presented by the simple act of swallowing sodium hydroxide. The immediate reaction is a marked inflammation and edema of any portion of the mucus membrane of the buccoesophageal tract with which the compound comes in contact. This produces an immediate dysphagia which disappears as the swelling subsides. A period of normal swallowing ensues until scar tissue formation produces a gradual obstruction of the esophagus. This obstruction manifests itself usually from two to three weeks after the original burn. The first indication is difficulty in swallowing solid foods. Then comes difficulty in swallowing fluids. If the stricture is complete there follows a severe dehydration and emaciation and eventually death by starvation. The mortality in the untreated cases is 50 to 60%. Those cases with a clearly defined stricture left untreated are always fatal.

A brief historical consideration of the treatment of strictures of the esophagus follows:

The earliest of these was blind bouginage. One method consisted of inserting a bougie made of elastic gum, stiffened by cooling, through the mouth and attempting to pass it through the stricture.

Concerning this method Fletcher in 1831, stated, "A firm stricture will turn it back and, if stiffened too much, it has all the mischief of the common bougie, for its point must be urged, and if placed wrong it may thus be drawn anywhere but through the stricture." Trousseau said, "Sooner or later all cases of stricture of the esophagus die of the bougie." These quotations are from Tucker.[2] Cases of mediastinitis from blind bouginage were reported as late as 1924, by Tucker.[2]

Mosher,[3] Plummer, Mixter and others pioneered in the work of using a swallowed string in treating esophageal strictures. The method consists of having the patient swallow a string, then threading the string through a fenestrated olivetipped metal bougie, pulling the string taut, then passing the bougie through the stricture using the string as a guide.

Jackson[4] advocated visualization of the stricture with an esophagoscope and bouginage through the esophagoscope. Mosher[3] also favored this procedure using ether anesthesia.

Internal esophagotomy and electrolysis are some peroral methods mentioned by Guisez[5] and others.

Retrograde Bouginage: The simple performance of a gastrostomy on these dehydrated malnourished patients was first done successfully in 1876, by Vernuil[6] in France on a 17 year old boy and was repeated a year later in Germany by Trendelenburg[6] on an eight year old boy.

Von Hacker[7] from Bilroth's Clinic in 1894, reported in considerable detail a procedure for dilating lye strictures. Previous to this time retrograde dilatations had been accomplished, but no one had thought to leave the string, with the ends tied together, in place between dilatations. Therefore, it was necessary to rethread the string through the esophagus either by having the patient swallow it and bringing it out through the gastric fistula or by doing a retrograde esophagoscopy and passing the string up from below.

Von Hacker's first paragraph is quoted directly as follows: "The procedure of dilatation of esophageal strictures after gastrostomy, designated by me as 'endless sounding' has already been carried out successfully in a number of cases." He was the first to advocate leaving the string in place between dilatations. His method consisted of first passing a string through the esophagus, then pulling a ruber drain tube stretched over a fish-bone-supporting rod halfway through the stricture, removing the rod and thus allowing the rubber tube to shorten and expand and so dilate the stricture. A string

was tied to each end of the rubber drain tube and after each dilatation the tube was removed and the string left in place with the ends tied together.

This "endless sounding" or continous string method, as it was subsequently called was also adopted by Guisez,[5] Ochsner[3] and others with various modifications.

Tucker[2] reported that he, Jackson and Clerf, one performing peroral and another retrograde esophagoscopy under biplane fluoroscopic guidance, had been able to penetrate complete esophageal strictures and pass a string. This procedure is also mentioned by Jackson in his textbook.[8]

Tucker[2] in 1924, published a continuous string method of retrograde bouginage using the rubber bougies designed by him. This procedure has stood the test of time and is certainly the method of choice in those patients where gastrostomy has already been performed, or where the strictures are so small as to prevent the passage of a mercury filled bougie perorally.

In those cases where it is difficult to pass an esophagoscope retrograde through the hiatus esophagus, the insertion of a cystoscope into the gastrostomy fistula, ballooning the stomach with water, and then passing a filiform catheter through the esophagus from below via the cystoscope facilitates the passage of a string. It is wise to have the patient's head slightly elevated during this procedure, otherwise water may find its way up the esophagus into the patient's mouth and be aspirated. It is best done under general anesthesia.

All of the above described procedures have to do with those cases of well established strictures of the esophagus. Treatment of recent lye burns of the esophagus has undergone radical changes in recent years.

Salzer[9] in 1920, and von Bokay in 1924,[10] were the first to advocate the *prevention* of stricture formation by the frequent early passage of mercury filled rubber bougies perorally. Bouginage of these recent lye burns of the esophagus begins several days after the ingestion of the lye, and is continued at daily and later weekly intervals for several months depending on the severity of the burn.

Martin and Arena[11] in 1939, and Gellis and Holt[12] in 1942, published papers confirming the original work by Salzer.

These same mercury filled bougies may be used in the cases of well established stricture as follows: After the stricture has been dilatated up to a No. 34 F or more retrograde fashion with a Tucker

dilator, the string may be removed, the gastrostomy closed, and dilatations continued perorally with a mercury filled bougie. After the stricture has been dilated by this method up to a No. 40 F the patient is instructed in the use of the bougie and is allowed to continue his dilatations at home. It is wise to have these patients return to the clinic once every six months for a barium swallow.

Occasionally one encounters a case of a well established stricture which fails to respond satisfactorily to either peroral bouginage with the mercury filled bougie or to the retrograde method with the Tucker bougie. These are the patients who continue to have recurrent episodes of complete obstruction despite adequate therapeutic measures, or have a complete stricture and so a permanent gastrostomy opening, or fail to dilate adequately from the beginning. Until recent years little hope could be offered these and they continued on as partial esophageal cripples. Since the advent of improvements in anesthesia, chemotherapy, antibiotics, and surgical technic and since blood from blood banks has become readily available, mortality in intrathoracic surgery has decreased to such a point that one may feel more confident about encouraging these patients to have esophagogastrostomy performed, in spite of the fact that the lesion is benign and the procedure rather formidable.

The following is a brief review of the history of esophageal resection and anastomosis:

The first successful resection of the thoracic esophagus for carcinoma was reported by Torek[13] in 1913. He did an esophagectomy, brought the proximal end out through the neck, and performed a gastrostomy. A rubber tube connected the esophageal fistula with the gastrostomy opening.

After esophagectomy has been performed re-establishment of continuity of the esophagus may be attempted by two methods, the antethoracic (as in Torek's case) or the intrathoracic (which more nearly simulates normal physiologic restoration).

Various methods of re-establishing continuity in the antethoracic procedure are as follows:

1. A skin-lined tube connecting the proximal fistula with the gastrostomy as advocated by Bircher in 1894.

2. Mobilization of the jejunum and anastomosis with the proximal stump of the esophagus as advocated by Cezar Roux and Yudin.[14] Colon (Kelling) and stomach (Kirschner) have also been mobilized to connect with the esophageal stump.

3. A combination of a tube graft and jejunum as mentioned by Yudin,[14] Longmire and Ravitch,[15] and others.

Various methods of re-establishing continuity in the intrathoracic procedure are as follows:

1. Mobilization of the jejunum after the principle of Roux and anastomosis with the esophagus as reported by Rienhoff[16] in 1946.

2. Mobilization of the stomach and the performance of an intrathoracic esophagogastrostomy. This was first proposed by Fischer[17] in 1926 and first performed by Decker[18] in 1935. Garlock[19] in 1940, and Churchill and Sweet[20] in 1942, and again Sweet[21] in 1946, reported cases of esophagogastrostomy for carcinoma of the esophagus.

As indicated, all of these cases had to do with carcinoma of the esophagus. More recently Sweet[22] in 1946, reported three successful cases done for esophageal stricture. He comments, "In cases of intractable stricture of the esophagus resulting from chemical burns, therefore, an esophagectomy followed by a high intrathoracic esophagogastric anastomosis is superior anatomically, physiologically, and psychologically to any form of external esophagoplasty as a method of restoring the functional continuity of the upper alimentary canal."

In 1949, Cecil[23] also reported three successful cases of simple lye burns on whom esophagogastrostomy was performed. He reported two other cases of lye strictures, with squamous cell carcinoma arising from the site of the stricture. On one of these a gastrostomy was done, the growth being too far advanced apparently for resection; on the other an esophageal resection followed by esophagogastrostomy was done. The immediate results were satisfactory.

A composite picture of the present-day methods of treatment is as follows:

I. Recent lye burns:

In the majority of clinics these are treated after the manner described by Salzer.[9] This method aims at the prevention of the formation of strictures by:

1) Neutralization of the alkali by a two per cent solution of acetic acid given orally. It has been argued that this does little good as the damage has already been done even if the interval between the swallowing and the treatment is short. We are convinced that it does no harm and it may do some good.

2) The insertion of a Levin tube at the time of the initial treatment. This has a two-fold purpose, it maintains a patent esoph-

ageal lumen, and offers a route for the administration of nourishment. It is left in place until peroral bouginage is begun, usually in two to four days. Gastric lavage may be carried out through the tube. This is included in the author's routine, because it lessens the possibility of stricture formation at the pylorus. Cases of pyloric stricture following ingestion of lye have been mentioned in the literature.[24]

3) The above procedures are usually performed in the emergency room. The patient is then admitted to the hospital (to the pediatric ward if a child) where the general state of health can be maintained and appropriate therapeutic measures instituted.

4) After several days, the patient (if a child, as is usually the case) is taken to the treatment room, restrained in a sheet and held, with the neck extended, sitting on a nurse's lap. A mouth gag is inserted and peroral bouginage is begun. Bougies graduated in size from a No. 14 F to a No. 40 F are used. Beginning with a No. 14, dilatations are continued up to the point where obstruction to its passage is noted and bleeding from the esophagus begins. The reason the esophagus is emphasized is because ulcerative lesions on the mouth and tongue will bleed at once due to trauma. These dilatations are continued daily for one to two weeks depending on the severity of the burn; then three times a week for one to two weeks; then once a week for several months. When the interval has been lengthened to once a week the patient is discharged from the hospital and dilatations are continued in the out-patient clinic for four to six months. If at the end of this time there is no difficulty in passing a bougie and no evidence of a stricture on fluoroscopic examination with barium, or esophagoscopy, the dilatations are discontinued and the patient is advised to return in six months for another barium swallow and fluoroscopy.

At the end of the first week a barium swallow and fluoroscopy is done. Esophagoscopy is occasionally done at this time if the attending thinks it is necessary. If it is performed, a general anesthetic is given and the esophagoscope is advanced only to the level of the most proximal lesion.

II. Lye Burns with stricture formation:

These patients invariably present a greater or less degree of malnourishment depending on the length of time the obstruction has been present and the extent of the obstruction. These patients are seen several weeks to several years after the burn. The author has two patients who were burned in childhood and did not develop obstructive symptoms until adult life.

If the malnourishment is severe (which is usual) the patient should be admitted to the hospital and fluids given intravenously. When the general physical condition permits, a barium swallow and fluoroscopic examination should be done and this should be followed by an esophagoscopy to confirm the diagnosis. If a stricture is demonstrated as the obstructor, then a gastrostomy should be done. After the wound has healed a string should be passed. String passage is usually attempted by the following methods and in the order named:

1. Have the patient swallow the string. This is best accomplished in the manner described by Tucker[3] as follows:

Introduce a string eight to ten feet long through the anterior naris into the nasopharynx. This is accomplished by tying one end of the string to a soft rubber catheter. A mouth gag is used, the tongue depressed, and the string and catheter grasped with forceps and brought out through the mouth. The string is cut and the catheter withdrawn. The cut end of the string is then re-inserted in the mouth with or without a lead shot attached near the end, and the patient is urged to swallow it using sips of water. The several feet of string remaining outside the nostril is wound on a piece of rubber tubing and attached to the cheek (arm cuffs may be necessary). This is unwound a foot at a time, passed through the nostril and the patient is urged to swallow it using sips of water, "all-day suckers" etc. If the string reaches the stomach it is brought out of the gastric fistula with a right-angled blunt retractor (of the Jackson type) or a right-angled gallbladder clamp. The two ends of the string are then tied together and retrograde dilatations using the Tucker bougies are begun. A period of twenty-four hours may be required for the swallowing to be accomplished.

If this procedure is unsuccessful under general anesthesia an attempt to pass a filiform catheter perorally via an esophagoscope is made. If successful, a thread is attached to the proximal end of the catheter and the distal end is lifted through the gastric fistula with a blunt curved instrument as above. The string is brought through, the ends are tied, and retrograde dilatations are soon begun.

If this is unsuccessful, retrograde esophagoscopy again using a filiform catheter, may be attempted. In the author's experience the location of the esophagus hiatus has been particularly difficult to find and therefore the utilization of the cystoscope to pass the filiform, preferably by a urologist as a consultant, has been the procedure of choice. As was mentioned above the patient is under ether

anesthesia, the body is held with the head elevated to about a 30 degree angle and the stomach is ballooned out with water.

Once a string is gotten through the stricture, no matter what method is used, and the ends tied together, retrograde dilatations are begun, using the Tucker bougies.

It will be noted that passing a fenestrated olive-tipped bougie over a swallowed string is not mentioned. The author feels that even though the retrograde procedure necessitates gastrostomy, it is much safer and, therefore, is the method of choice.

After the stricture has been dilated up to a No. 34 to a No. 38 F by the retrograde method, the string is removed and peroral dilatations are begun with a mercury-filled rubber bougie. After a No. 40 is reached the patient or his parents may be given a No. 40 bougie, instructed in its use, and advised to continue the dilatations at home once a week. They are advised to return every six months to the clinic for a barium swallow and fluoroscopic examination.

In patients in whom it is impossible to pass a string and the gastrostomy must be maintained permanently, or those who won't dilate beyond a No. 30 to No. 32 F, or those whose strictures contract down again rapidly after either retrograde or peroral bouginage, (especially those who have been adequately dilated by the retrograde method and whose patency cannot be maintained by peroral bouginage after closure of the gastrostomy) or those patients who develop mediastinitis after dilatation; it is necessary to refer them to a thoracic surgeon for esophagogastrostomy after the manner described by Sweet et al.

Case No. 1.—H. L. N., chart No. 80450, a colored male two years of age, was admitted to Roper Hospital on August 13, 1949, at 10:30 P. M. He was accompanied by his mother who stated that about 4:00 P. M. the afternoon before the child had drunk a solution of lye, which the mother intended using to scrub the floor. The mother gave him eggwhite and rubbed some lard in his mouth. The child then began to vomit up some whitish material but no blood. He was taken to a neighboring hospital a short while later where an attempt was made to make the child swallow some lemon juice. This met with little success. The child returned home and had not been able to swallow liquids or even saliva during the past twenty-four hours because of the swelling of mouth and lips.

Previous history was essentially negative as was the family history.

CASES ADMITTED TO ROPER HOSPITAL SINCE 1943

TABLE I

AGE INCIDENCE

Age 1 - 2	22 or 63%
Age 2 - 5	11 or 31%
Age 5 - 20	1 or 3%
Age over 20	1 or 3%

TABLE II

TYPE OF TREATMENT		DURATION OF TREATMENT
Salzer	20 or 56%	All under 3 mos.
Retrograde	15 or 44%	All over 6 mos.

TABLE III.

RACE

White	2 or 6%
Negro	33 or 94%

TABLE IV

GASTROSTOMY REMAINED OPEN	(44% of total cases had gastrostomy)
Under 3 mos.	1 or 1.3%
3 - 6 mos.	
6 - 12 mos.	1 or 1.3%
Over 12 mos.	13 or 41.4%

Physical examination was essentially negative except for marked edema and multiple ulcerative lesions of the lips and mouth. These lesions were covered with a whitish exudate. Much saliva was present drooling from the mouth.

Immediate treatment consisted of the intramuscular injection of 300,000 units of penicillin and the passage of a Levin tube. The penicillin was continued at daily intervals. The patient was fed by Levin tube until August 17, 1949, when the tube was removed and the esophagus dilated by the passage of mercury filled bougies from a No. 12 through a No. 30 F. He had some difficulty swallowing and retaining what little he did swallow during the next twenty four hours, so the Levin tube was re-inserted.

He was dilated through a No. 40 F the following morning (August 18, 1949) and after this had no difficulty with oral feedings.

The esophagus was dilated through a No. 40 F at daily intervals through August 22 (i.e. for six dilatations). No difficulty was encountered in passing the mercury filled bougie at any time during the dilatations. After the first six dilatations at daily intervals he was dilated three times a week until September 23, 1949. He was discharged to the clinic for weekly dilatations on September 27, 1949.

A fluoroscopic examination with a barium swallow on September 8, 1949, showed a mild narrowing of the esophagus throughout its middle third. Multiple small niches were seen in the walls of the involved segment. This was repeated on October 26, 1949, and showed the previously described narrow segment to be more sharply limited to an area of about 3 cm in length situated over about the sixth thoracic vertebra. No significant dilatation above this lesion and no obstruction to the passage of the barium was noted.

Weekly dilatations in the clinic have been accomplished without difficulty. All dilatations after the first one were through a No. 40 F.

CASE No. 2.—H. B., chart No. 74201, a colored boy 17 months old was admitted to Roper Hospital December 11, 1948. His father stated that he was apparently well until one month before admission at which time he was discovered playing with an open can of Red Devil lye and was seen to put the can to his mouth. Shortly thereafter the oral cavity including the tongue and the roof of the mouth "turned white and was sore for about a week." After a week it was noted that the patient would swallow solid food which was "coughed up" (regurgitated) soon after swallowing. This condition had grown progressively worse. However, the patient was still able to swallow

liquids. The bowel movements which had previously been normal in consistency and one to two a day had now become hard and he had one only every other day.

The previous and family histories revealed no abnormal findings.

The physical examination revealed a broncho-pneumonia on the left and a barium swallow revealed a constriction in the lower third of the esophagus. It was impossible to pass a No. 10 F mercury filled esophageal bougie.

The patient was treated with antibiotics and responded very nicely. His fluid intake was sufficient to maintain his nourishment and he was discharged on December 18, 1948, with the understanding that he would return in several weeks for a gastrostomy.

He returned on January 24, 1949, and a Janeway type gastrostomy was done on January 25, 1949. His ability to swallow even liquids had worsened considerably in the intervening month. His recovery was uneventful. He was discharged to the clinic for retrograde dilatations on February 3, 1949.

He was re-admitted on February 7, 1949, because the string which he had previously swallowed had become lost during a retrograde dilatation. The string was re-inserted the following day under ether anesthesia. This was accomplished by inserting a filiform catheter perorally, retrieving it from the stomach, using a cystoscope, tying a string to the distal end and drawing it through. The patient was discharged the following day.

Retrograde dilatations at weekly intervals have continued in the clinic. The patient is now up to No. 38 F.

CASE NO. 3.—W. W., a 7 year old colored male, chart No. 19929, was admitted to Roper Hospital June 5, 1943. He gave a history of having swallowed a solution containing lye when he was two years old. Shortly thereafter he was unable to swallow nourishment and a gastrostomy was done at another hospital. He has learned to take care of his gastrostomy and feeds himself, but on account of this handicap is not as active as other children his age. He was admitted to the hospital so that an attempt could be made to dilate the esophagus.

Family history and previous history were essentially negative.

Physical examination showed a moderately well developed, but rather poorly nourished colored boy with no other abnormal findings except a well functioning gastrotomy wound with a tube present in the wound.

Fluoroscopic examination on June 9, 1943, with a swallow of barium showed the barium to descend in the esophagus to the level of the sternal notch. The impression of the examiner (Dr. B. Kalayjian) was: "Complete atresia of the esophagus at the level of the sternal notch, cause undetermined."

Serology was negative, urinalysis and blood counts were within normal limits.

On June 10, 1943, under general anesthesia peroral and retrograde esophagoscopy was done, but complete obstructions were encountered after advancing the esophagoscope a short distance (3 to 4 cm) within the proximal and distal esophageal orifices. Not even a ureteral catheter would pass.

An attempt to pass a ureteral catheter retrograde using a McCarthy cystoscope was made under ether anesthesia by Dr. William H. Prioleau. This too was unsuccessful.

The patient was discharged (Edgefield, S. C.) on June 24, 1943, two weeks after admission without much having been accomplished except to demonstrate that he had a complete esophageal obstruction.

He was re-admitted November 7, 1945. Fluoroscopic exam on November 10, 1945, again showed a complete esophageal obstruction on attempting to swallow barium "at the level of the inferior margin of the second thoracic vertebra."

On November 17, 1945, he was seen by Dr. H. G. Smithy in consultation. On that date under a general anesthesia, Dr. Smithy attempted to pass a ureteral catheter up from below using a McCarthy cystoscope. This too was unsuccessful.

On November 26, 1945, under ether anesthesia Dr. Smithy did a transgastric exploration of the esophagus. The stomach was opened and the esophageal orifice was located and brought under direct vision. Many attempts were made to pass ureteral catheters, esophageal bougies, and assorted types of metal instruments through the esophagus, but a complete obstruction, encountered about two inches within the esophageal orifice, prevented their passage. The postoperative course was uneventful.

Having met with so little success in our efforts, it was decided to refer him to Dr. L. H. Clerf at Jefferson Hospital, Philadelphia. Dr. Clerf agreed to accept him and he was transferred to that hospital on December 10, 1945, directly from Roper.

A personal communication from Dr. Clerf is quoted as follows:

"Studies were carried out by means of double plane fluoroscopic table using peroral bouginage and bougie introduced by retrograde esophagoscopy. So far as could be determined the upper segment of the esophagus was stenosed at the level of the third thoracic vertebra. A bougie passed by retrograde esophagoscopy was observed to go up to the fifth thoracic vertebra suggesting that the defect is considerable extending from the third to the fifth.

"Because of this extensive defect it was decided to carry out an open operation. Thoracotomy using a right side posterior incision, was performed and the esophagus exposed. It was found intimately adherent to the surrounding tissues. It was separated and then with bougies (olive tipped metal bougies) in both upper and lower esophageal segments the surgeon was able to guide these and to separate the esophagus from surrounding structures so that ultimately it was possible to pass the lower bougie upward for a distance of three and one-half inches. At this point there was a definite barrier which corresponded to the bottom of the pouch of the upper segment. Forward grasping forceps were introduced from above through the esophagoscope and under digital guidance it was possible to penetrate this barrier without penetrating the esophageal wall. A string introduced from below was grasped with forceps and the patient's esophagus was threaded in this manner. He made a prompt and satisfactory recovery from this procedure and retrograde bouginage was instituted. When discharged in August, 1946, retrograde bougies up to and including size 18 were passed."

He was discharged from Jefferson Hospital on August 24, 1946, a little more than nine months after admission.

Retrograde dilatations were continued at the clinic at Roper and later, arrangements were made for them to be continued in Columbia, S. C. which was nearer his home. He was dilated using Tucker retrograde bougies No. 38 to No. 40 F for many months. The gastrostomy was finally closed at Edgefield, S. C. in June, 1949, approximately eleven years after the ingestion of the lye. The author is informed that his subsequent progress has been satisfactory.

CASE NO. 4.—O. M., chart No. 5913, a colored female, 19 years old was admitted to Roper Hospital August 13, 1947. She stated that since April, 1947, following the birth of a child she had had considerable trouble swallowing solid food. Frequently she would have to "wash" bread, etc. down with water. She frequently has had to take laxatives. She has lost ten to twelve pounds in weight since the onset of her symptoms.

Her past history and family history were negative. Serology was negative as were other laboratory examinations including gastric analysis and a B M R.

A chest x-ray taken before admission (July 21, 1947) revealed a negative chest. Fluoroscopy with a barium swallow also before admission revealed: "The upper third of the esophagus was normal. The middle third was curved posteriorly in an arc and there was a fairly uniform compression for about 6 cm, causing a uniform flattening of the esophagus by extrinsic pressure, Barium passed constantly through this area, but slowly. The impression was retrocardiac lymphadenopathy or possibly a lymphoid tumor with adherent esophagus. Recommend that the patient be returned for two oblique views of the chest." This was done on August 14, 1947, and showed no mediastinal mass.

An esophagoscopy was done August 16, 1947, and revealed an obstructive narrowing in the lower third. A biopsy was done and microscopic examination revealed a chronic esophagitis.

A flouroscopic examination with barium swallow was repeated on August 25, 1947, and the same findings of compression in the middle third were noted. The impression at this time was sideropenic dysphagia.

Esophagoscopy was repeated on August 27, 1947, by Dr. Edward Parker of the surgical staff with the author present. Our conclusion at that time was that despite the negative history, the appearance resembled that of a lye stricture. Biopsy was repeated and microscopic examination again revealed chronic esophagitis.

She was discharged to be dilated in the clinic with mercury filled bougies perorally. These dilatations continued until February 22, 1948, when swallowing became more difficult. She was readmitted to the hospital and esophagoscopy and biopsy were repeated. Again the pathological report showed only chronic esophagitis.

Another consultation with Dr. Parker was obtained and he advised esophagogastrostomy. This the patient refused. She was discharged, improved, February 26, 1948.

Peroral dilatations were continued in the clinic until June 22, 1948, when she was admitted for twenty-four hours for another esophagoscopy under sodium pentothal anesthesia by Dr. Parker. A concentric narrowing was encountered at the 30 cm level. No biopsy was done.

On July 9, 1948, the patient was again admitted to Roper Hospital, this time for exploratory thoracotomy and possible resection

of the stricture. This procedure was performed by Dr. Parker on July 13, 1948. At operation it was found that the stricture, by palpation, extended for a distance of 8 cm, much longer than was suspected by x-ray. In view of the length of the stricture it was not considered that it could be resected and an end-to-end anastomosis performed. Therefore, the wound was closed without performing the anastomosis at that time. The postoperative course was complicated by an atelectasis of the left lung which required bronchoscopic aspiration. She was discharged in good condition on July 24, 1948.

The patient continued to have progressive difficulty in swallowing. She was re-admitted on January 9, 1949, and on the following day an attempt was made to pass a pneumatic dilator, but this met with no success. Following this the patient was advised to have a gastrostomy done and retrograde dilatations. She agreed and this was performed on January 11, 1949. A previously swallowed string was retrieved from the stomach at the time of operation. She made an uneventful recovery and was discharged on January 17, 1949, to return to the clinic for retrograde dilatations.

Retrograde dilatations continued until September, 1949, at which time she was being dilated through a No. 38 F. The dilatations are being done perorally using mercury filled bougies No. 32 to No. 32 F. The string has been removed. If the patency is maintained for several months we contemplate closure of the gastrostomy and occasional peroral dilatations. Her appetite is good, she has no difficulty swallowing, and has regained her weight loss.

COMMENT

Four cases are presented in some detail which are illustrative of the various types of treatment, methods of placing the string, and the results to be expected with these.

The first case demonstrates the shortened hospital stay, the simple procedures employed, and the excellent state of nutrition maintained by the patient when the formation of strictures is prevented by the employment of the Salzer technic.

The second case illustrates one method of placing a string in a case with a well formed stricture.

The third case shows what may be accomplished even when the esophagus is completely obstructed. In view of recent improvements in surgical techniques, this patient would probably be advised to have an esophagogastrostomy if he were seen at this time.

The fourth case shows how confused the picture may become if a clear cut history is lacking. If this case continues to have progressive dysphagia an attempt at esophagogastrostomy will probably be made.

CONCLUSIONS

These cases require the cooperation of the entire hospital staff.

These cases occur mostly in children between the ages of two and five years, and these patients are usually in the lower economic brackets. Any method which will shorten the hospital stay will lighten the financial burden on the community.

The Salzer method of early dilatation, which prevents stricture formation in recent lye burns, requires the shortest period of hospitalization of any method developed to date, and produces the most satisfactory end results.

Preliminary gastrostomy followed by retrograde dilatations using the Tucker bougie is the method of choice for those cases of well established stricture.

Where the patient does not respond well to retrograde dilatations or where it is desired to shorten the length of the treatment, recent improvements in technic have made esophagogastrostomy the procedure of choice.

SUMMARY

An historical review of lye burns of the esophagus and their treatment is presented.

Pertinent facts regarding thirty-five cases seen in the past six years at Roper Hospital are presented in table form.

Four cases are presented in detail to illustrate the various types of treatment employed. Comment is made on the cases and conclusions are drawn.

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III

INTERNAL LARYNGOCELE

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Laryngoceles are conveniently divided into three catagories: internal, external, and combined internal-external. Many of the papers dealing with this subject include descriptions of operations on the external or combined external-internal types. On the Head and Neck Service at Memorial Hospital two cases of internal laryngocele have been observed; in one of these the sac has been successfully removed through an external surgical approach.

HISTORICAL NOTE

Air sacs which take origin from the larynx and retain communication with its cavity are rare anomalies long recognized in man. Larrey,[12] in 1829, made note of cystic, air-filled tumors in the necks of blind men employed to make the calls to prayer from the temple towers in Egypt, and to their presence he ascribed a progressive voice impairment which eventually reduced the men to labor on the temple grounds and fish ponds. Bennett,[2] in 1865, exhibited an abnormally developed larynx, not known to have been present during life, in which he discovered the first air sacs demonstrable in man, and Virchow,[22] in 1867, reported the occurrence of unusual degrees of dilatation of the ventricles of the larynx which he had independently observed and designated as laryngoceles.

Subsequent descriptions to which known reference has been made still provide accounts of less than 70 cases of laryngeal air sacs in man.

CASE REPORTS

Case 1.—R. O'G., a 57 year old Irish-American laborer, came to the hospital in August, 1942, because of intermittent hoarseness

From the Head and Neck Service of Memorial Hospital, New York City.

Fig. 1.—Appearance of internal laryngocele by mirror laryngoscopy. The swelling overhangs the vocal cord and pyriform sinus and distends the aryepiglottic fold.

of about three months' duration. His past history was irrelevant. His hoarseness had appeared insidiously and had recurred without known cause for varying periods each day.

No general findings of significance were noted at the initial physical examination. By indirect laryngoscopy a smooth, nonulcerated swelling, 3 cm in diameter, was discovered in the region of the left aryepiglottic fold, bulging into the cavity of the larynx as well as into the pyriform sinus (Fig. 1).

Two weeks later, because of an area of erosion in the vicinity of the left arytenoid, a biopsy was done, which was reported negative for neoplasm. Puncture of the tumor led to its immediate collapse and subsequent roentgenograms (Fig. 2) confirmed the clinical impression of laryngocele.

For the next two years, aside from hoarseness, the patient had no serious symptoms until enlargement of the sac finally caused symptoms of laryngeal obstruction. A tracheostomy was done as a preliminary to extirpation of the laryngocele, but a series of postoperative cardiac and pulmonary complications ensued which prevented further surgery. A tracheostomy tube is still worn by the patient, corked by day and open at night, and no further alteration of the air sac has been observed.

Case 2.—M. S., a 54 year old white man, a foundry helper of Irish-American descent, came to Memorial Hospital on May 1, 1945, because of dyspnea and hoarseness of about sixteen months' dura-

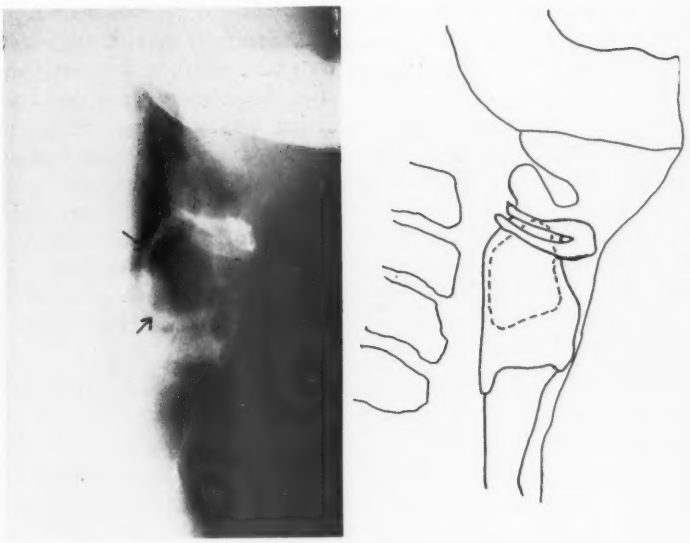


Fig. 2.—Lateral x-ray of the larynx showing the internal laryngocele, which is outlined in dotted lines on the tracing to the right.

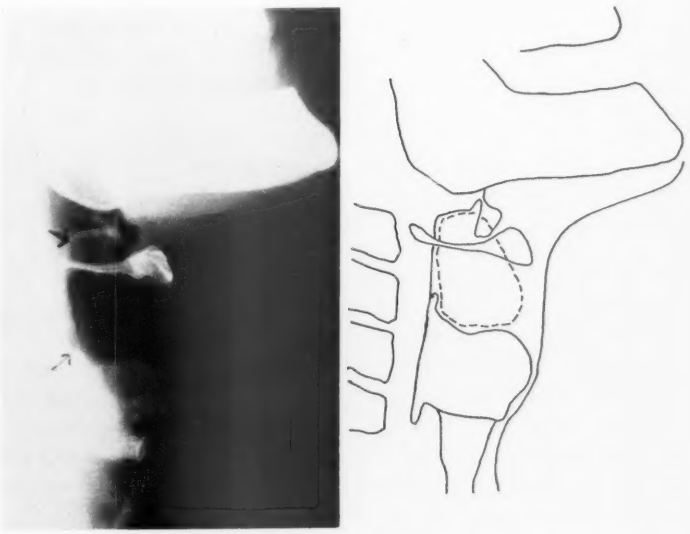


Fig. 3.—Lateral x-ray of the larynx showing internal laryngocele rising well above the level of the hyoid bone. Dotted lines in the tracing indicate the limits of the air sac.

tion. His past history was irrelevant. The hoarseness had been noted in the course of an infection of the upper respiratory tract, and it soon had been accompanied by orthopnea and by persistent dryness of the throat. The advice of a physician was requested six months later, and therapeutic irradiation was suggested when examination of the larynx seemed to show that cancer might be present. This treatment was accepted by the patient, and during the ensuing month a total dose of 3500 roentgens (200 kv, 70 cm TSD, 1 mm Cu, 6x8 cm portals, 250 r x 2 per dose) was administered through each of two cervical portals. Considerable improvement followed this procedure, but within a month the symptoms had recurred. The patient then was referred to Memorial Hospital for further care.

No findings of significance were noted at the general examination. By indirect laryngoscopic study, a smooth non-ulcerated tumor four or five centimeters in diameter was discovered filling the left pyriform sinus and encroaching on the lateral pharyngeal wall. It's appearance was essentially the same as that in the first case (Fig. 1). The diagnosis of laryngocele was made and roentgenographically confirmed (Fig. 3), and operative treatment advised.

A lateral approach was chosen, with removal of the posterior third of the thyroid cartilage, since the greatest swelling by mirror examination appeared to be in the region of the arytenoid, with the margins overlapping the cord medially, the pyriform sinus laterally and extending upward and forward into the aryepiglottic fold. On January 31, 1946, a preliminary tracheostomy was done through a low midline incision under local anesthesia. Then under intravenous pentothal a traverse incision was made in the skin at the upper margin of the left thyroid cartilage from the midline to the anterior margin of the left sternomastoid muscle (Fig. 4). This was carried down to the infrahyoid muscles which were split longitudinally to expose the thyroid cartilage. The perichondrium was incised (Fig. 5) and the posterior third of the cartilage was dissected free and amputated (Fig. 6). The laryngeal vessels and superior laryngeal nerve were retracted. At this point the bulge of the laryngocele could be seen through the thyrohyoid membrane and it became apparent that removal of the left wing of the hyoid bone would facilitate matters, because the swelling ascended beneath the hyoid. The infrahyoid muscles were therefore reflected downward, the grater cornu dissected free from its bed and amputated near the midline (Fig. 7).

Incision through the thyrohyoid membrane exposed the laryngocele itself, which was carefully dissected free from the aryepiglottic fold without entering the larynx. In descending to its origin

at the ventricle, the sac entered the larynx from above rather than from posteriorly, so that a V-shaped section was excised from the superior edge of the thyroid cartilage (Fig. 8). This enabled us to expose the neck of the sac and to ligate it close to the ventricle. After the sac was amputated, the wound was closed in layers and a small penrose drain was inserted. The latter was removed the following day and healing was uneventful.

The tracheostomy tube was removed on the ninth day and the patient discharged. He has been examined at frequent intervals since then. Both cords can be seen. There is some limitation of motion on the operated side and persistent edema of the arytenoid, possibly due to the effects of the radiation which he received. The voice is slightly husky, but there is no impairment of the airway.

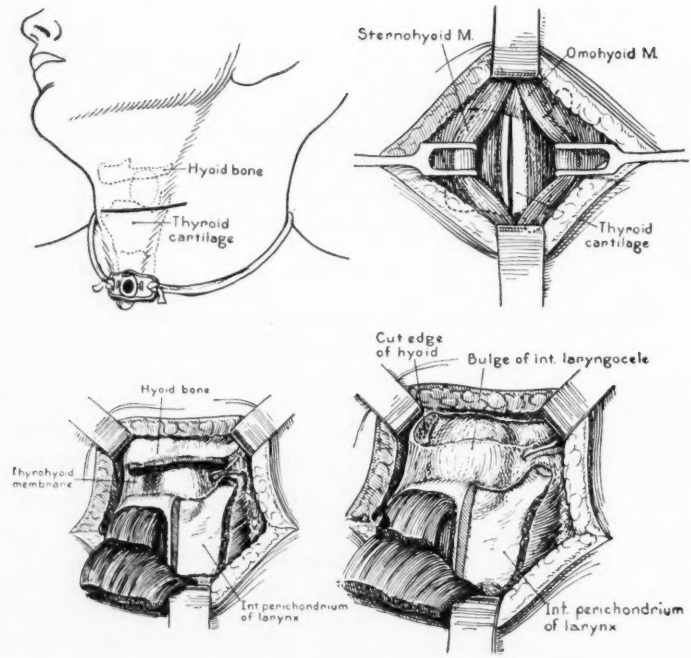
Inspection of the gross specimen showed a very narrow tract which entered the sac tangentially and admitted a small probe only after considerable search. This may explain the ease with which air becomes entrapped in laryngoceles. Section of the sac revealed psuedostratified columnar epithelium on a fibrous stroma infiltrated by lymphocytes.

ETIOLOGY

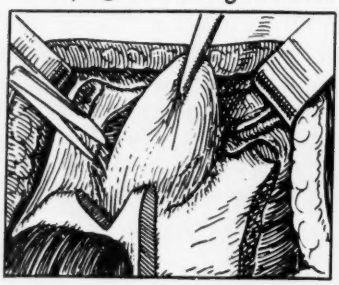
Incidence. Air sacs rising higher than the upper border of the thyroid cartilage exceed the limits of normality which Virchow arbitrarily defined, and provide a favored site for further pathologic change. Distention of their cavities follows each appreciable increase in intraglottic pressure resulting from some such exertion as chronic coughing, excessive and violent use of the voice, the efforts associated with glass-blowing and with the playing of wind instruments and certain other prolonged or strenuous muscular activities. Extension of the sac to the tissues of the neck may be aided by a deficiency or weakness of the thyrohyoid membrane accompanying its penetration by the superior laryngeal nerve and blood vessels. Edema of the orifice of the sac may also promote its distention and, by obstructing drainage, contribute to subsequent infection.

Age and Sex. Most air sacs have been found in men, and most men thus afflicted have been of middle age or older. Explanation of their predilection hinges on the cause and circumstance of increased intraglottic pressure and presupposes repeated interaction of various aggravating factors in the presence of senescent tissue change.

Anatomic Considerations. The ventricles of the larynx, where all laryngoceles arise, were first recognized by Galen,[7] and careful studies of their structure were first afforded by Morgagni[17] and



Laryngocele being dissected



Laryngocele ligated

Fig. 4.—Operation for removal of internal laryngocele. Incision from midline of neck to anterior border of sterno-mastoid muscle at level of upper border of thyroid cartilage. Preliminary tracheostomy under local anesthesia.

Fig. 5.—Infrahyoid muscles split to expose thyroid cartilage. Perichondrium of latter incised and stripped from posterior third.

Fig. 6.—Posterior third of thyroid cartilage removed. Superior laryngeal vessels and nerve identified and preserved. Sternohyoid, omohyoid and thyrohyoid muscles severed at their attachment to hyoid and reflected downward.

Fig. 7.—Hyoid bone dissected from its bed and amputated at midline, permitting better exposure of internal laryngocele.

Fig. 8.—Thyrohoid membrane has been incised, the sac has been isolated from the aryepiglottic fold and a notch has been cut in the superior border of the thyroid cartilage to facilitate exposure of the neck of the sac as near to the ventricle as possible.

Fig. 9.—Sac ligated. After amputation the neck retracted downward within the larynx.

Hilton.[9] Few observations which have since been made are much at variance with these earlier descriptions, and papers individually prepared by Lindsay,[14] Allman,[1] Moore[16] and Freedman,[5] are essentially compendia of this subject.

Gross Anatomy. The normal ventricle is a deep elliptical recess horizontally placed between the vocal cord and the ventricular band, and is entered by a narrow slit-like aperture just superior to the cord. Limiting it above is the crescentic, overhanging margin of the ventricular band, and serving as its boundaries laterally and below are the membranous portion of the vocal cord and the various fasciculi of the thyroarytenoid muscle. Ballooned above a tiny orifice found anteriorly in its wall is an elongated diverticulum or sacculus which rises vertically to occupy a pocket between the thyroid cartilage and the base of the epiglottis. Lattice-like fibers of the thyroarytenoid muscle contribute to its lateral and medial support. It is from the extension of this sacculus that laryngoceles are formed.

Microscopic Anatomy. The lining of these pouches is a ciliated, pseudostratified columnar epithelium with a fragile basement membrane. The walls are fibrous strands of tissue which support a network of minute blood vessels and an array of mixed mucous, tubloacinose glands encircled by fasciculi of nonstriated muscle. Goblet cells are present in somewhat variable number, and lymphoid cells in isolated clumps are found dispersed haphazardly through the stroma.

Developmental Anatomy. The ventricle and sacculus have been identified by Frazer[4] in the eighth week of embryonic life as definite, active outgrowths from the larynx, set apart from all the visceral clefts and placed immediately above the nodules which become the vocal cords. Within the first year they have usually grown to form comparatively swollen sacs. According to Galatti,[6] the sacculus normally loses its capacity for further growth by the sixth year, while the ventricle acquires a deeper cavity and then enlarges slowly until it attains adult proportions approximately two years later.

Morbid Anatomy. The classification of laryngoceles as internal, external, or combined internal-external depends on the relationship of the sac to the thyrohyoid membrane. If it is entirely within this boundary, it is internal; if it is present only in the neck at about the level of the hyoid bone, it is external; and if it can be observed both by laryngeal examination and by scrutiny of the neck, it is of the combined type. Conversion of the internal type into the combined

probably occurs if the causative factors are continually exerted over a long period of time.

Considering the rarity of laryngoceles and the almost universal existence of factors which impose a rise in intraglottic pressure, one must presuppose the anlage of a laryngocele in those individuals in which the condition actually develops.

SYMPTOMS AND CLINICAL COURSE

Impairment of the voice occurs most frequently as the first symptom of laryngocele, and alteration ranging from slight change in quality or pitch to unremitting hoarseness or aphonia has been reported. Cough may be a prominent complaint, and later in the course of the disease dyspnea may become the dominant symptom. This has even led to asphyxia. Both of our patients customarily emitted a sound like a belch before beginning to speak. This we attributed to expulsion of air from the sac by voluntary contraction of the pharyngeal constrictors.

If the sac is small and little or no strain is placed on it by excessive coughing or by repeated and prolonged rise in intraglottic pressure, no change may occur, and aside from a slight modification of the voice the patient will be asymptomatic. However, increase in the size of the sac from one cause or another will result in increasing dyspnea in the case of internal laryngocele, in an enlarging compressible cervical mass in external laryngocele, and in one or both of these things in the combined type, depending on the location of the greater swelling.

The possibility, first of asphyxia, and second of infection in the sac, requires that these swellings be taken seriously and the proper treatment be instituted. Otherwise one would place them in the category of medical curiosities.

DIAGNOSIS

Almost invariably the correct diagnosis of laryngocele is not made at the initial examination. Other more common tumors are usually suspected, especially cysts and unless one notes the unusual compressibility of the lesion it may be some time before the true nature of it is established.

In the external or combined type collapse on gentle pressure of the fingers will occur, the sac refilling in variable periods of time, depending on the amount of intraglottic pressure exerted by the patient and on the size of the channel leading into the sac. Palpation of an internal laryngocele is more difficult, but the observer

may take note of the soft compressibility of the swelling when he touches it with the tip of a laryngoscope or with a probe.

X-ray studies will frequently establish the diagnosis by disclosing an ovoid area of radiolucency in the region of the clinical swelling. The internal type is more readily seen in a lateral view, partially overlying the vallecula, epiglottis or larynx. The external variety shows up better in an antero-posterior exposure, as the radiolucent area is superimposed on the muscles of the neck. The antero-posterior view of the internal laryngocele may be unsatisfactory because of superimposition of the sac on the air column of the hypopharynx.

Finally aspiration which leads to immediate collapse of the sac is pathognomonic of laryngocele. If one obtains purulent or mucoid fluid, however, one may be misled into thinking that an infected laryngocele is only an abscess or infected cyst.

TREATMENT

The care of air-sacs which cause symptoms is inevitably dependent on skilled surgical attention. Relief of urgent dyspnea may require puncture of the sac, a hazardous procedure without laryngoscopic observation, and imminent asphyxia may demand laryngeal intubation or immediate tracheostomy. In the presence of infection only necessary measures such as relief of dyspnea, should be employed.

When operation may be safely undertaken, total extirpation of the sac is indicated. Attempts at destruction of the sac by cautery or partial excision through the laryngoscope are foredoomed to failure because of the impossibility of eradicating all of the lining membrane. Similiarly an attack on the tumor through a laryngofissure is open to criticism on the basis of excessive intralaryngeal scarring with consequent impairment of the voice and possibly laryngeal stenosis.

A vertical division of the thyroid cartilage extended to expose the aryepiglottic folds has been used by Hansberg[8] and has been advised by Lewis[13] and by Freedman.[5] Our experience with this approach leads us to believe that resection of the posterior third of the thyroid cartilage may be unnecessary in certain cases and that notching of the superior border of the cartilage is advisable to allow dissection of the neck of the sac to its point of origin in the ventricle. Removal of the homolateral half of the hyoid bone is essential if the tumor is of any size. A preliminary tracheostomy and general anesthesia are prerequisite to the smooth handling of such a case.

In one of our patients a full course of high voltage radiation was administered before the patient came to Memorial Hospital, on the assumption that the swelling was due to cancer of the larynx. No attempt was made to biopsy the lesion and the result was damage to normal tissues which interfered with healing to the extent that the patint has a persistent edema of the aryepiglottic fold on the operated side. Such indiscriminate use of radiation therapy should be avoided.

SUMMARY

1. Two cases of internal laryngocele with hoarseness and difficulty in breathing are presented.

2. A surgical approach for removal of an internal laryngocele is described and illustrated.

3. Etiology, symptoms, diagnosis and treatment are reviewed.

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IV

CURARE AS AN ADJUNCT TO RELAXATION IN ESOPHAGOSCOPY

A REPORT OF 55 ENDOSCOPIES IN 53 PATIENTS

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Few physicians would presume to take issue with Jackson,[1] the pioneer in all forms of endoscopy, in most matters in that field, but a good many would not agree with him that what he called "the sermon on relaxation" is all that is essential, in addition to an empty stomach, for successful esophagoscopy. For myself, I willingly grant that I may lack his persuasiveness, but my own experience has frequently been that something more may be needed. Some patients simply do not lose their nervousness and apprehension under any amount of preoperative explanation and reassurance, while others in this group, in the intensity of their desire and attempt to cooperate, tie themselves, so to speak, into even tighter knots.

These patients have always presented a problem. Some of them have flatly refused to submit to esophagoscopy, even under anesthesia. In others, when I realized their temperaments and anticipated difficulty, it was my practice to resort, without further ado, to general anesthesia, at first with ether and later with sodium pentothal. Still later I began to use curare in combination with sodium pentothal, for the reason that sodium pentothal, while it produces unconsciousness, does not inhibit reflex muscular activity which is the desideratum in esophagoscopy. It also has the additional disadvantage that because of its stimulating effect on the parasympathetic nervous system, its use may be associated with laryngeal spasm and with respiratory difficulties manifested by hiccoughs, sneezing and coughing. None of these measures, furthermore, took care of the patient whose physique and build made for difficulties in esophagoscopy. I

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refer, of course, to the obese patient whose neck, like the rest of his body, is short and thick.

The excellent muscular relaxation secured when curare was used with sodium pentothal suggested that it might be adequate in itself for the performance of esophagoscopy. The results in the first few cases in which it was tried were so satisfactory that for the last three years I have used this method in all cases in which I had reason to believe that simple topical analgesia would not be sufficient for a satisfactory examination.

The situation which the esophagoscopist encounters when he introduces his instrument is more or less that described by Jackson for bronchoscopy. For the introduction of the light and delicate bronchoscope, he notes that it is necessary first to introduce a laryngoscope, which is necessarily of heavy, strong construction to overcome the powerful muscles of the tongue, the pharynx, and some of those of the neck. The introduction of the bronchoscope, in other words, involves the overcoming of the obstacles set up by powerfully contracting muscles.

The introduction of the esophagoscope involves the overcoming of the resistance offered by much the same muscles. In addition, even if, as Jackson words it, it is insinuated rather than introduced, there is another major point of resistance to overcome, at the level of the cricopharyngeus muscle. In some cases there is still another, though minor, point of resistance, at the hiatus esophagus, where the pull of the diaphragmatic musculature on the crura is felt. These are tonically closed points, at both of which what amounts to a pinchcock mechanism is operative. In effect, however, the nervous, apprehenive patient creates a series of tonically contracted points all along the pathway of the esophagoscope, and the patient with a short, thick neck, however cooperative he may desire to be, presents similar points of resistance.

HISTORICAL NOTE ON CURARE

The accounts recently published on the development of curare[2-4] are so complete that not many details need be given here. The story, as Cullen[3] well puts it, is both humbling and fascinating. The Indians of South America, who were well aware of the properties of this drug, tipped their arrows with it and thus paralyzed their prey before they closed in for the kill. Sir Walter Raleigh, in a voyage up the Orinoco River in 1584, in what is now British Guiana, was the first white man to observe its effects. When he returned to England he brought some of it to Queen Elizabeth, along with his other trophies and gifts. The first scientific study of the drug, however, was not

made until 1857, when Claude Bernard determined that it acted on the neuromyal junction, a structure which is just what its name implies. Experimental studies have since amply confirmed his theory that the paralysis which curare produces is caused by interruption of the neuromuscular mechanism.

The clinical possibilities of curare have been realized for many years. It seems first to have been used by Hoffman, in 1879, but he gave such a large dose to the patient he was treating for tetany that tracheotomy as well as artificial respiration was necessary. The dangers inherent in the use of curare, which this experience so well exemplified, kept it a laboratory agent, employed chiefly in physiologic and pharmacologic studies, until 1938. Then Richard C. Gill, who had lived for many years in the upper Amazonian jungles of Equador, brought back adequate supplies of curare, from a known source, and thus made it possible for a pharmacologic house (E. R. Squibb & Sons) to manufacture accurately assayed extracts which could be safely used clinically. Up to this time the variations in the pharmacologic and physiologic effects of the various preparations had been so great, and the side-effects so dangerous, that the clinical use of curare could not be justified. Each cubic centimeter of intocostrin has a physiologic activity equivalent to 20 units of curare and contains the equivalent of 20 mg of a standard extract.

Since 1938, when the first purified preparation (intocostrin) was introduced, curare has been used for many purposes. In that year Burman[3] administered it to overcome muscle spasm and rigidity in spastic paralysis and dystonia musculorum deformans. In 1940, Bennett[3] presented at the American Medical Association an exhibit on the use of curare in metrazol shock therapy, to prevent the traumatic complications which so frequently accompany convulsive shock therapy. Lewis Wright,[3]who saw the exhibit, persuaded Harold Griffith of Montreal that intocostrin might be a valuable adjunct to anesthesia, and in 1942 Griffith and his associate, Enid Johnson,[8] reported its use for this purpose in 25 patients. Since then curare has been used in many thousands of cases, not, of course, as an anesthetic but as a supplemental agent to secure muscular relaxation. Ophthalmologists have found it extremely useful for this purpose, as Boles'[5] recent report shows, and Robertson[6] has recommended it as an adjunct agent in tonsillectomy under sodium pentothal.

THE RATIONALE OF THE USE OF CURARE IN ENDOSCOPY

It is easy to understand why ophthalmologists and otolaryngologists should find curare so useful: Its effect is selective. Its first

action is on the small muscles of the head, face and throat, this selective action being explained possibly by the fact that, as Comroe and Dripps[4] point out, fine muscles receive impulses over the motor nerves at a more rapid rate than do the coarse muscles. It is also extremely fortunate from the standpoint of therapeutic usefulness, as the same authors note, that the intercostal and diaphragmatic muscles, which are essential for respiration, are affected last of all.

The first report on the use of curare to facilitate endoscopy was made by Cullen and Trapasso[7] in 1943. It covered 29 procedures in 16 patients, including esophagoscopy five times, esophageal dilatation eight times, and bronchoscopy or Lynch suspension in the remaining cases. Although the authors concluded that the method was useful in patients in whom endoscopy, for one reason or another, was difficult, the complications which they encountered seemed to invalidate their conclusion. Thus intercostal paresis developed in nine cases, laryngospasm in four, and complete respiratory paralysis in two. The paralysis in each instance lasted only two or three minutes and was readily controlled by artificial respiration, but this is an alarming occurrence, no matter how quickly it is overcome, as I can testify from my single experience with it. My own explanation of Cullen and Trapasso's difficulties lies in the dosages which they used. Fifteen of their patients received more than 40 mg (2 cc) of intocostrin, of whom 2 received 70 mg each and 2 received 100 mg each. It is true that three patients who received only 20 mg each had undesirable reactions, and it is also true that eight patients who received dosages of 45 mg or over had no reactions at all, but many of the dosages which these authors employed were a good deal larger than I would choose to use, and I am inclined to believe that many of their difficulties rose from that circumstance. It is also only fair to point out that they were the first to use intocostrin for endoscopic purposes.

In 1944 Silverberg and Ansbro[8] reported 21 endoscopies on (20 patients), four of which were esophagoscopies. Poor results or complete failures, from the standpoint of muscular relaxation occurred in four cases. Five patients, of which three became cyanotic and had convulsions, required resuscitation. The authors understandably concluded that curare was not a satisfactory or safe drug for endoscopy because its results were unpredictable, and because it was difficult to determine the exact dosage for the individual patient. Myerson, who discussed the paper, agreed that the drug was not necessary, safe, practical or valuable in endoscopy, and concluded by saying, "I would summarize my remarks by saying that if bron-

choscopy had to be done with curare, I would prefer not to perform bronchoscopy."

I am aware of only one other article dealing exclusively with the fore, aware of only one other article dealing exclusively with the use of curare in endoscopy, this being Lorhan and Roberts'[9] 1947 publication on combined curare-sodium pentothal for bronchoscopy and laryngoscopy. In the 27 cases in which they used this method, they secured good relaxation in 26. The remaining patient developed severe respiratory depression and had to be resuscitated with neostigmine methylsulfate. These observers did not share Silverberg and Ansbro's fears about the dangers and ineffectiveness of curare, or Myerson's even gloomier conclusions. They felt, in fact, that when the drug is used in small dosages (their own upper limit was 3 cc) and with the proper precautions, it is a safe and effective agent.

INDICATIONS AND CONTRAINDICATIONS FOR THE USE OF CURARE IN ESOPHAGOSCOPY

My own use of curare in esophagoscopy is strictly limited to patients in whom, for any reason, I expect the procedure to be difficult. In my private practice I use it for nervous, apprehensive patients. On my service at Charity Hospital of Louisiana at New Orleans, I have found it particularly useful for negroes and for patients of French and Italian descent. All of these patients are inclined to be excitable and emotional, and they prove nervous and uncooperative when only topical analgesia is used, even though premedication has been adequate. It is not possible to perform a satisfactory esophagoscopy when a patient is thrashing about on the table or is completely rigid and unrelaxed, and I no longer try. On both my public and private services I also use curare for patients with short, thick necks who, for physical reasons, regardless of their nervous and emotional status, are always difficult to examine satisfactorily.

I would emphasize that I have never used curare, nor do I intend to use it, to extend the indications for esophagoscopy. This is still a procedure to be used with caution, if at all, in patients with aneurysms impinging on the esophagus, and in patients who are dyspneic and hyertensive or whose vital capacity is reduced, regardless of the reason. Curare would not overcome the dangers of esophagoscopy. under these circumstances. As for the drug itself, the only really important contraindication to its use seems to be myasthenia gravis, which it would aggravate because the clinical manifestations of this disease are, in effect, the results which curare itself produces.

The first advantage of curare as an adjunct to esophagoscopy is that it eliminates the need for general anesthesia, which formerly had to be employed whenever topical analgesia was not sufficient. This is a highly desirable state of affairs. General anesthesia, by whatever agent it is secured, is unsatisfactory for esophagoscopy unless it is deep, and anesthesia on a deep plane, however skilfully it may be given, has always seemed to me to be unfortunate for such a short procedure: The risk may be minimal, but it still exists. Sodium pentothal, in spite of its advantages, is a dangerous anesthetic for esophagoscopy: Even when it is carefully used, profound respiratory depression may ensue before the patient is sufficiently relaxed for the examination to be performed with facility. The risk is minimal, but again it exists. Avertin is useless for esophagoscopy because it causes spastic muscular contractions and increases the reflexes. Finally, the substitution of the barbiturates is no more satisfactory than is their use in preanesthetic medication. They excite some persons, particularly older persons, and I prefer not to use them at all for endoscopy.

TECHNIQUE OF ADMINISTRATION OF CURARE

The secret of success, as well as of safety, in the administration of curare for esophagoscopy is careful attention to every detail. The fundamental precaution is that the drug is administered by a competent anesthetist whose sole duty is to administer the curare, watch the patient, and give oxygen without a moment's delay if it should be needed. I have never used curare, nor do I intend to, without this set-up. This is positively not a method which the endoscopist should attempt to handle himself. Esophagoscopy is sometimes a simple procedure but sometimes it is not, and every time it is carried out the operator needs to devote his full attention as well as both his hands to the manipulation of the instrument and to careful investigation of the esophageal canal.

Preoperative preparation consists, as in the usual case, of the administration of morphine and atropine, the dosage being regulated according to the patient's weight and age. For the 150-pound adult the usual dose is ¼ gr of morphine and 1/150 gr of atropine, given 30 minutes before the time set for the operation. I do not omit the preoperative medication in any patient regularly scheduled for esophagoscopy, but I have not given it in an occasional night emergency and have managed very well without it.

Before the operation is begun, the usual precautions are taken to see that the esophagoscopic set is entirely ready, that duplicate parts are at hand, that oxygen is ready for administration, and that the

anesthetist and the assistant are in their places and ready to carry out their assigned functions. Attention to these details is essential in all esophagoscopies and is particularly essential when curare is used because its effects are of such short duration that there is no time for delay if they are to be utilized.

The patient is placed on the operating table in the usual position for esophagoscopy and the throat and larynx are anesthetized with whatever local anesthetic agent may be preferred. My own preference is for a solution made up of cocaine crystals (4.0 gm), adrenalin (5.0 cc, 1:1000 solution), 2 per cent potassium sulfate solution (25.0 cc) and enough 0.5 per cent phenol solution to make 100 cc. Within 15 minutes of its application this solution produces very satisfactory analgesia. I have performed esophagoscopy many times without anesthetizing the throat and larynx, but the procedure is so much simpler, and so much pleasanter for the patient, when it is used that I see no point in omitting this step.

At the appropriate signal the anesthetist introduces into the cubital vein the predetermined dose of curare in the form of intocostrin. For the adult weighting 150 pounds an injection of 1 cc (20 units) is given over a period of 30 seconds by the clock. At the end of two minutes by the clock, the patient is asked to raise his head. If he cannot, esophagoscopy is proceeded with by the usual technique. If he can lift his head, an additional injection of 1 cc of curare is given, again over a period of 30 seconds by the clock. This dosage is exceeded only if the increase is justified by the patient's size, and in no case is more than 3 cc given.

The anesthetist does not leave the operating room until the entire procedure is concluded. An occasional patient has asked to walk back to his room, and has been permitted to do so, but the usual patient is returned to bed by roller. He is kept in the hospital —esophagoscopy is, of course, never performed anywhere else—for six to eight hours. My own preference is to perform the operation early in the morning and keep the patient in the hospital until three or four o'clock. No special postoperative treatment, in the way of drugs, diet, posture or anything else, is required.

If esophagoscopy is a scheduled, elective procedure, it is my custom to tell the patient that we intend to give him an injection to make him more comfortable during the operation. I doubt that otherwise most patients would know that they were being given the drug, especially since we have learned to avoid the diplopia, which is an unpleasant, if harmless, experience, by covering one eye with a small pad before the curare is given. I usually cover the left, merely

because I am right-handed and the pad on that side is not disturbed by my movements. In the small dosages used, the weakness of the eyelids and of the muscles of the throat and jaw, the inability to swallow or cough, and the weakness of the arms, legs and intercostal muscles which follow the use of larger dosages of curare are not experienced.

Comroe and Dripps[4] call attention to the fact that the effects produced by a single injection of curare wear off clinically within 20 minutes, as judged by determinations of the tone of the abdominal musculature, but that electromyographic recordings indicate that the full effects do not disappear two to four hours. They warn, therefore, that a second large dosage should not be given within a period of four hours. The warning is sound, though it is obviously not relevant to the method which I am describing.

Sensitization to curare is a possibility, and, therefore, if it is given a second time, the patient should first receive a skin test. No reaction of this sort was observed in the patient in my own series who had curare three times, but my recollection is that it has been reported when curare was used more than once as an adjunct to shock therapy.

If respiratory paralysis or respiratory difficulties of any kind occur, artificial ventilation with oxygen is generally preferred to prostigmine, which is the antidote to curare. This method was promptly successful in the single case in my own series in which its use was indicated.

ANALYSIS OF CASES

Over the past three years I have used curare 55 times in 53 patients as an adjunct to esophagoscopy for pathologic and traumatic conditions of the esophagus and related structures. Twenty-one of the operations were performed at Charity Hospital of Louisiana at New Orleans, and the remainder in my private practice at Our Lady of the Lake Sanitarium in Baton Rouge.

The Charity Hospital patients were distributed as follows:

Sixteen negro men, ranging in age from 30 to 70 years, of whom 6 were over 60 and 7 others were between 50 and 60 years of age.

Seven negro women, ranging in age from 19 to 72 years, of whom 3 were 60 years of age or over and another was 52.

Two white men, aged 49 and 60 years, respectively.

Three white females, aged 34, 40 and 54 years, respectively.

The private patients were distributed as follows:

Sixteen white men, ranging in age from 19 to 77 years, of whom 3 were 60 years of age or over and 2 others were between 50 and 60 years.

Twelve white women, ranging in age from 18 to 68, of whom 2 were over 60 years of age. All the others were under 46 years of age.

The figures are, of course, too small to be in any way significant, but the preponderance of older persons in the Charity Hospital patients, particularly in the male patients, is worth mentioning. Many of these men were feeble and debilitated and any sort of struggle or excitement would have been extremely undesirable.

The esophagoscopies were performed for the usual reasons. In the younger group the chief indications were lye and other burns of the esophagus, with cardiospasm the reason in an occasional case. In the older group the chief indications were dysphagia, hematemesis, carcinoma and extrinsic tumors. Both the older and the younger groups included a number of instances of suspected foreign bodies, which in ten cases were actually found to be present and were removed. Chicken bones and dental plates were the most usual objects found, and in two instances the dental plates had lacerated the esophageal mucosa. Two patients, both negro men, were esophagoscoped to confirm the presence of suspected diaphragmatic hernias, which in both instances were present.

Relaxation was excellent in every case, and in only one of the 55 operations was there any untoward reaction. This patient, a 60-year-old negro man with a diaphragmatic hernia, was unable to breathe for three minutes after he had been given 2 cc of curare. Normal respiration returned promptly when he was given artificial respiration under positive pressure with the anesthesia machine and the examination was carried out without further difficulty. One patient, a 50-year-old negro man, was esophagoscoped three times, each time with the aid of curare, over a period of a month, for suspected carcinoma of the esophagus. The first two biopsies were reported negative, but the clinical evidence was strongly in favor of malignant disease, and on the third examination a piece of cancerous tissue was secured.

The excellent results and the negligible incidence of reactions in these 55 esophagoscopies can be attributed to the careful administration of curare and the small dosages used. Two patients received 1.5 cc, 22 received 2 cc, and two both large negro men, received 3 cc each. The remainder of the patients received 1 cc. These

dosages were all well within the limits of safety and, for the purposes for which they were used, they were entirely adequate. In other words, there is no need to use a dangerous, large dosage of curare, and no justification for using it, in the performance of esophagoscopy because entirely satisfactory muscular relaxation can be accomplished with a safe, small dosage.

In the majority of these esophagoscopies curare was used because the patient was known to be nervous, excitable or apprehensive, or his temperament suggested that he might become so in the course of the examination. In six instances the patients were obese and their short, thick necks made adequate exposure impossible under topical analgesia alone; three weighed more than 200 pounds.

SUMMARY AND CONCLUSIONS

By a sort of clinical evolution curare has come to be substituted for general anesthesia to secure satisfactory muscular relaxation in nervous, apprehensive patients or in patients with short, thick necks, in whom the examination would otherwise be difficult or impossible. It has not been used to extend the indications for esophagoscopy. The drug is administered by a competent anesthetist, in small dosages (1-3 cc), with oxygen available for immediate use if respiratory difficulties should develop. Curare employed with these precautions has proved both safe and satisfactory. The essential details of 55 esophagoscopies performed on 53 patients are briefly summarized.

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V

SCLEROSIS OF THE ANTRUM

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The term "Sclerosis of the Antrum," to our knowledge, has never been used in the literature to designate any of the osseous affections of the maxillary sinus. We have chosen this term for the entity to be discussed to differentiate it from the other osseous lesions of the maxillary sinus.

Complete or partial osseous absence of the maxillary sinus may occur because of some disturbance of the normal development of the sinus, or may be due to pathologic changes occurring after a normal sinus has developed. The maxillary sinus is the most constant of the nasal accessory sinuses, and is rarely found to be partially or completely absent. When this condition is found, it may be difficult to differentiate as to whether it is acquired or developmental in origin.

ACQUIRED CONDITIONS

The acquired osseous lesions which have been reported to produce complete or partial bony obliteration of the maxillary sinuses are:

1. *Paget's Disease of the Skull.* This is one of the more common affections of bones first reported in 1877. It occurs usually after the age of forty and is thought to be due to some local disturbance in bone metabolism. The disease is characterized in its early stages by absorption of bone, which is succeeded by an osteoblastic phase in which there may be progressive thickening of the bones of the skull. The roentgen picture is characteristic, even before any deformity has appeared; however, the sclerotic lesions of Paget's disease may be confused with other hyperostoses. The picture varies with the phase in which the disease is seen. After the stage of primary softening, in which bone is replaced by fibrous tissue, the bone be-

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comes hard and thicker, for ossification predominates, and there is a heavy deposit of subperiosteal, finely porous, cancellous bone on the skull making the surfaces rough and irregular. The affected bones are thick and dense. It is unusual for Paget's disease to involve the maxilla but this has been described in the literature. Brailsford[1] points out that the maxillary sinus may be considerably expanded, although the entire cavity is ultimately obliterated by the marked calvarial thickening. Childrey[2] and others have reported complete obliteration of the maxillary sinuses with Paget's disease of the skull.

2. *Monostotic and Polyostotic Fibrous Dysplasia.* This is a predominantly unilateral fibro-osseous lesion involving one bone (monostotic form) or many bones (polystotic form). This name was suggested by Lichtenstein[3] in 1938 to clarify the existing confusion regarding fibro-osseous disease. Previously this condition was described as osteitis fibrosa, fibrosarcoma, giant cell tumor, ossifying fibroma, osteodystrophy, etc. In this condition the interior of the bone is found to be filled mainly by gritty grayish-white fibrous tissue containing trabeculae of newly formed primitive bone. It manifests itself in childhood or early adult life and evolves slowly. The first sign of the disease is usually a local swelling of the skull, ribs or tibia. When the skull is affected, the maxilla is the most common bone involved. According to Pugh,[4] the lesions in the frontal, sphenoid, ethmoid and maxillary bones are different than those found in other parts of the cranium or long bones. In these regions the bone appears to be densely sclerotic instead of having the cystic appearance with some sclerotic areas as is seen with other bones. He refers to this as an osteomatoid change caused by fibrous dysplasia of the bone since the density of the bone is often as great as that of an osteoma. The bone is abnormally thick, with external deformity often present, and the paranasal sinuses are frequently completely or partially obliterated. However, in the cases of fibrous dysplasia reported by Cooke and Powers,[5] and others, the maxillary sinus was obliterated by the same gritty grayish-white fibrous tissue containing bony trabeculae which is found with involvement in other parts of the skeleton. The cause of the disease is unknown. It was originally described by Lichtenstein and Jaffe[6] as resulting from a perverted activity of the specific bone forming mesenchyme. Another theory holds that the condition is due to endocrine dysfunction; and recently, Schlumberger[7] expressed the opinion that trauma was a cause.

3. *Leontiasis Ossea.* This is a clinical, descriptive term and not a pathologic entity. It is used to describe those cases of hyperostosis of the skull whose nature is not understood. The forms of

leontiasis ossea were well described by Knaggs[8] in 1923 and are as follows:

a. Creeping Periostitis of the Facial and Cranial Bones. This is a form of hyperostosis beginning almost always in the nasal fossae or paranasal sinuses. It is characterized by an exuberant deposit of subperiosteal bone, especially on the facial bones, and the slowness with which the process passes from bone to bone. The general plan of extension is influenced by the attachments of the periosteum. Where that membrane dips between adjacent bones, as at the suture lines, the process is held up for some time. The periostitic bony deposit accumulates and forms a heaped up, bulging, and sometimes almost overhanging edge. Then the process finally invades the adjacent bone. The sinuses most often attacked and obliterated are the maxillary, the frontal and the sphenoidal. Nearly always the corresponding sinuses on both sides are involved. In addition to obliteration of the sinuses, massive deformity of the facial bones may occur. Cases of complete or partial obliteration of the maxillary sinus due to creeping periostitis have been reported by Virchow, Cooper, Pagel, Horsley, and Stanley, according to Knaggs.[8]

b. Circumscribed Osteitis. This form of leontiasis ossea involves one or more of the cranial bones. It usually begins as a localized swelling, shading off into normal bone. It gradually invades the whole bone, and then it may spread to involve adjacent bones. This circumscribed form usually begins in the frontal bone, and, rarely, may invade the maxilla and maxillary sinus. Horsley[8] pointed out that in this form the outer surface of the swelling is smooth and the diseased bone presents a marked contrast to the normal, being notably more vascular and its surface pitted with minute foramina.

c. Localized Osteitis. This type of hyperostosis was originally described by Westmacott[9] in 1913 under the heading of "Chronic Hyperplasia of the Maxilla." It is unilateral and is localized either in the maxilla or less commonly in the mandible and rarely spreads to other bones. The alveolus is first attacked and then the outer wall of the maxilla towards the malar process is involved to produce a characteristic deformity of the maxilla. The deformity consists of a unilateral smooth swelling of both walls of the alveolus, especially the external wall, the swelling being prominent in the canine fossa. In all of Westmacott's cases, the maxillary sinus was invaded early and the whole antral cavity was filled with a very vascular cancellous type of bone. Knaggs[8] also reported numerous cases of localized osteitis of the maxilla, all of these cases showing partial or complete obliteration of the antrum. In the majority of the cases re-

ported, there have been associated dental abscesses in the region of the hyperostosis.

The etiology of leontiasis ossea is unknown. Knaggs thinks the most probable cause is a micro-organism, the infection traveling under the periosteum and setting up an osteitis of the adjacent bony tissue. Von Recklinghausen thought that trauma was a factor and, in fact, a history of trauma is frequent in the cases reported. Ziegler thinks that the disease is due to a congenital disposition of the periosteum and marrow to grow. Freedman,[10] Pugh,[4] and Falconer[11] regard the cases of leontiasis ossea which have been reported as cases of fibrous dysplasia. The view that leontiasis ossea is a special form of Paget's disease has also become popular. The roentgenological findings of leontiasis are characteristic, showing deforming enlargement of the bones, narrowing of the medullary portion throughout localized areas of the skull and face, and secondary narrowing of the orbits and sinuses.

4. *Obliterative Sinusitis.* This entity was originally described by Skillern[12] in 1936 as being a partial or complete obliteration of the frontal sinus cavity of one side by osteogenesis. No external deformity of the bone is present, thus differentiating this from the other forms of acquired osseous lesions of the sinuses. The osteogenesis begins in the anterior wall of the frontal sinus and extends back toward the posterior wall, producing a thick, eburnated type of bone which may extend to the posterior wall and completely obliterate the sinus cavity. In Skillern's[12] cases, numerous pockets were found within this new bone in which infection had persisted, as shown by cultures. Therefore he expressed the opinion that obliterative frontal sinusitis is due to infection. According to Sluder,[13] the hyperostosis may start as a sequence of an ordinary hyperplasia of the mucous membrane, the infection forming a stimulus of irritation to the granulations in the diploic spaces. These, according to Furstenberg,[14] are converted into fibrous connective tissue, which may be followed by the development of a dense layer of compact bone. The periosteum beneath the infected lining membrane may be so traumatized by the disease that it becomes congested and thickened and assumes the appearance of granulation tissue. This serves as a young connective tissue base of an embryonic character in which ossification may follow. The connective tissue elements rapidly multiply with a differentiation of some of the cells into osteoblasts. Thus, there is formed an interlacing framework of trabeculae which is at first uncalcified and is spoken of as osteiod tissue. The latter is soon infiltrated with calcium salts and there are formed numerous trabeculae, or spicules of bone, completing the process of ossification.

The ossification is always limited at the intersinus septum. Obliterative sinusitis is differentiated from failure of development of the frontal sinus by roentgenograms, which reveal a definite outline of the previous cavity of the frontal sinus. Also mucous membrane was always found during operative intervention in the cases of obliterative sinusitis. The only known reported cases of obliterative maxillary sinusitis have been those cases of obliteration of the maxillary sinus by cancellous bone following radical antrum operations.

5. *Von Recklinghausen's Disease, Acromegaly, Syphilis, and Xanthomatosis.* These rarely produce complete osseous obliteration of the maxillary sinus, according to Collins,[15] Freedman,[10] Pancoast,[16] and Brailsford.[1]

Even though the etiology of all of the above types of hyperostosis is indefinite, they are all conditions acquired later in life after a normal antrum has already developed. It is our purpose to differentiate these acquired osseous lesions of the maxillary sinus from two cases of sclerosis of the maxillary sinus which we believe to be developmental in origin.

CONGENITAL DEVELOPMENTAL ANOMALIES

Nature has designed a program of development for the pneumatized spaces of the mastoids and the paranasal sinuses and experiences suffered by these parts during the period of their formation are reflected in their growth and development. The maxillary sinus begins as an outpouching of the mucous membrane of the lateral wall of the ethmoidal infundibulum and it continues to grow until the eighteenth year by a process of pneumatization and encapsulation. The ethmoid sinuses are also present at birth, though they are only rudimentary. As a rule the frontal sinuses begin as a bud or cell nest projecting into the frontal bone from the anterior ethmoid cells. Thus when the ethmoids become diseased, either by infection or allergy, growth usually ceases in the frontals as well as the ethmoids. During the first year the maxillary sinus occupies an anterior position beneath the orbit, and the sinus rapidly increases in size as the first dentition progresses. Shea[17] has pointed out that if pneumatization is arrested, such as at the area above the canine tooth, the bone remaining at the base of the canine socket will be diploic in form. This is of particular importance in reference to our cases. The maxillary sinus is the most constant of the nasal accessory sinuses and is seldom absent. Davis[18] mentions reports by Reschreiter of four cases in which a maxillary sinus was absent.

There have been many conflicting reports regarding the factors which bring about and influence pneumatization of the paranasal sinuses. Killian expressed the belief that the development of sinuses depends on inherent biological characteristics of cells which make up this area. Coffin and Freres[19] and others have explained the pneumatization of sinuses on a physical basis, the bone resorption supposedly being due to variations in air pressure, particularly that of expiration, since the principle growth of the sinuses occurs after breathing begins. Richter[19] stated that the stimulus for pneumatization goes out from the mucous membrane and that since some sinus development occurs in fetal life, air pressure as an influencing factor is out of the question.

Grahe[19] in 1931 did experimental work with rabbits to find some factors influencing development of the nasal sinuses. He took out the molar teeth of six young rabbits and sewed up the external nares on one side in six more rabbits. Four months later the corresponding antra were undeveloped in the six rabbits whose molar teeth had been extracted. The rabbits whose external nares had been sewed up showed no abnormalities of antral development. Grahe inferred that growth of the alveolus is the principle influence on the development of the antrum.

Tanturri[20] said that he felt certain from his study of adults and of newborn infants with poorly developed sinuses, and from his experimental work on animals, that trauma at birth or in infancy causes a retardation in the development of the sinuses. After varying degrees of traumatization of experimental animals, he was able to demonstrate extravasations and inflammatory exudates extending into the centers of ossification. After three or four months, the affected sinus was definitely underdeveloped as compared with the opposite side.

Mortimer[21] found that disturbed pituitary function during the postnatal period may cause partial or complete obliteration of the maxillary sinus. In his experiments, hypophysectomy on dogs and rats was found to produce aplasia of the bone marrow. The process of simultaneous central resorption of bone and peripheral deposition of calcium ceases. The frontal, sphenoidal and maxillary sinuses cease to grow. If the animal is allowed to survive many months, calcium is added to the inadequately expanded bony structures so that a relative increase in density or sclerosis of such bone results.

Shea[17] stated that heredity is the greatest factor in determining the size and shape to which sinuses are destined to develop. How-

ever, Shea[22] also expressed the opinion that a single severe infection or multiple mild infections may arrest the growth of the sinus. The infection, if limited to the anterior ethmoid cells, will influence these cells and possibly prevent the migration necessary for the development of the frontal sinuses, which normally occurs in the second year. The maxillary sinuses may be involved alone.

Rosenberger[23] roentgenologically studied 163 private patients who had evident or suspected sinus infection with a view toward determining whether sinus infection affects sinus growth. He found that 53% had symmetrical frontals, while 87% had symmetrical antra; 10% had infected frontals, whereas 74% had evidence of antrum infection; 9% had aplasia of one or both frontals, while there was no instance of an absent antrum. On the basis of this data, he concludes that, "As a general rule sinus aplasia is not a sequel of sinus infection, though such a relationship may occasionally occur, hence the Wittmaack theory of altered mastoid pneumatization may not appropriately be applied to explain altered sinus pneumatization."

CASE REPORTS

CASE 1.—M. Z., a 31 year old white male, was first seen on November 11, 1946, complaining of a cough of several months duration. The patient stated that his nose had been "stopped up" for the past several years and there was a history of slight postnasal discharge for several months. There were no headaches, facial pain or excessive nasal discharge. The past history was negative except for a tonsillectomy and adenoidectomy performed in childhood. Examination revealed the ears, nasopharynx, throat, teeth and cervical glands to be essentially negative. Examination of the nose revealed the septum to be deflected anteriorly to the right, with a long obstructive ledge along the left floor. The mucosa was moist and somewhat injected. The turbinates were mildly turgescent. There was a small amount of mucoid discharge on each floor, but no discharge was obtained on suction. All sinuses were black to transillumination. The x-ray report by Dr. Howard H. Ashbury reads as follows: "The frontal sinuses are either absent or rudimentary. There is a marked increase in density over all of the sinuses, and this is believed to be due to both thickening of the lining mucous membrane and polyposis" (Fig. 1).

The patient was advised to have a submucous resection, bilateral ethmoidectomy and radical antrostomy. He was admitted to the hospital on November 25, 1946. Laboratory studies of the blood and urine were all normal. On November 26, 1946, a submucous

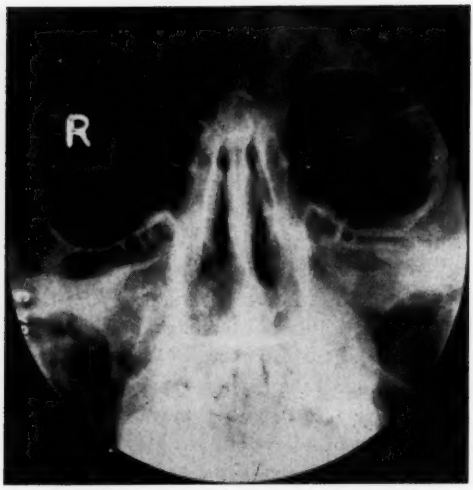

Fig. 1.—Pre-operative x-ray of Case 1, showing undeveloped frontal sinuses and sclerosis of the antrums.

resection was performed under local anesthesia. Upon entering each ethmoid labyrinth, the bony septa were found quite hard, the cells were unusually small and no polyps were found on either side. The patient was then anesthetized with sodium pentothal and a Caldwell-Luc operation was performed on the right side. Upon removing a dense, hard anterior bony antral wall in the canine fossa, no antral cavity could be demonstrated. Instead, the entire region of the antrum was filled with a hard diploic type of bone, and no mucous membrane was discernable anywhere. By careful curettement the bone was found quite firm and spongy, and a considerable quantity of it was removed so that a cavity was created which, though somewhat smaller than a normal adult antral cavity, was of similar outline. A large nasoantral window was made through dense hard bone and the antrum was packed with iodoform gauze tape, the end of which was placed so as to protrude into the nose through the nasoantral window. In view of the findings in the right antrum, and the similar x-ray appearance of the left antrum, it was decided not to operate upon the left antrum.

The postoperative course was complicated by an acute sinusitis involving the newly created right antrum, and this persisted in spite of local therapy, sulfadiazine orally and penicillin intramuscularly.

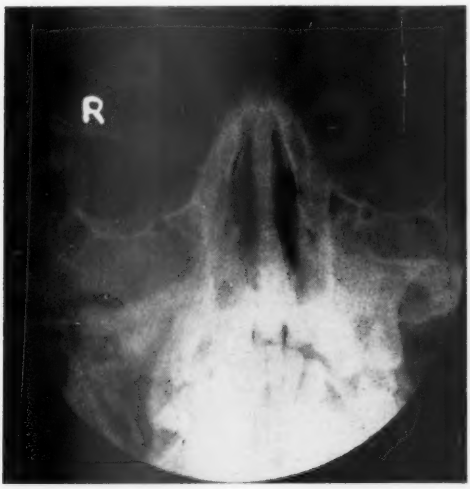

Fig. 2.—Post-operative x-ray of Case 1, showing complete regeneration of bone and obliteration of the right antrum again.

The patient required treatment until March of 1947, before he could be discharged. Just prior to discharge, his sinuses were again x-rayed, and the following report was made of them: "The antra are both densely cloudy and there is no evidence of a cavity in either one. The ethmoids are clearer than in the previous examination, prior to operation" (Fig. 2). It was felt that the bone had regenerated and completely filled the right antrum, and attempts to irrigate the antrum through the nasoantral window confirmed this impression.

CASE 2.—F. B., a 45 year old white female, was first seen on October 8, 1949, with a complaint of headaches with pains over the eyes and in both cheeks for 15 years. The past history was negative except for a tonsillectomy and adenoidectomy performed ten years ago. Examination of the ears, throat and cervical glands was negative. Examination of the nose revealed an obstructive spur on the septum posteriorly. The mucosa was injected and edematous, and there was some mucopus in each side, but none was obtained on suction. The vault of the nasopharynx was essentially clean, but there was considerable lymphoid hyperplasia around each tubal orifice. There was complete adentia with prosthesis. The following is a report of the x-rays: "The frontals and sphenoids are small but clear. The ethmoids and antra show a marked increase in density caused by thickened membrane and possible polyps" (Fig. 3).

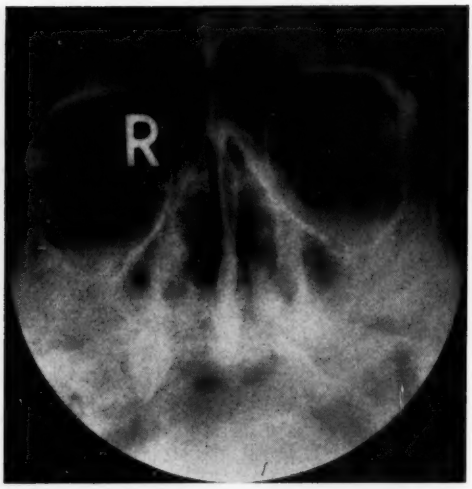

Fig. 3.—Pre-operative x-ray of Case 2, showing sclerosis of the antrums.

The patient was advised to have a bilateral ethmoidectomy and radical antrostomy. She was admitted to the hospital on October 20, 1949. Laboratory studies of the blood and urine were all normal. On October 21, 1949, under local anesthesia, a submucous resection and bilateral intranasal ethmoidectomy were performed. Upon entering the ethmoid labyrinths, the bone was found to be extremely hard and sclerotic and the cells were unusually small (almost absent) and no polyps were found. The patient was then anesthetized with pentothal, and a right Caldwell-Luc operation was begun. Upon removing the thick, dense, anterior bony antral wall, no antral cavity was found. Instead, the entire region of the antrum was found to be composed of dense, hard sclerotic bone. No mucous membrane was discernible anywhere. In view of the experience with the previous case, the oral mucosal incision was closed without removing the bone from the "antrum," and it was decided not to operate upon the left antrum, which exhibited a similar picture by x-ray.

In retrospect, both of these patients had general skeletal features which are usually associated with endocrine imbalances, especially of pituitary disfunction during the growth periods of the individual. The patients were somewhat smaller in stature than usual, had "square" faces with prominent chins and jaws, and rather prominent supra-

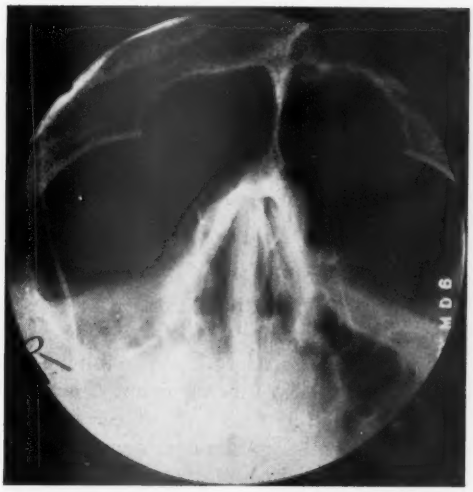

Fig. 4.—X-ray demonstrating osseous obliteration of the right maxillary sinus following radical antrostomy.

orbital ridges and eyebrows. There was a rather abundant growth of hair in both, so that even the woman had a visible beard growth.

COMMENT

The acquired osseous lesions of the maxillary sinus must be differentiated from the developmental osseous lesions. The main point of differentiation, clinically, consists of the presence or absence of the outline of the bony margin of the maxillary sinus roentgenologically. In cases of acquired osseous obliteration of the antrum, the outline of an adult antrum should be discernable on careful examination of the x-ray; whereas in cases of developmental origin, if any outline is present, there will only be the outline of a very small, rudimentary, infantile cavity.

A careful general medical examination, including roentgen examination of the skull and long bones, is essential in these cases in order to rule out generalized bone pathology. An accurate history must be obtained to rule out chronic sinusitis as the possible cause of osseous obliteration of the sinus. At operation, in cases of acquired osseous obliteration of the sinus, some of the mucous membrane lining of the original antrum should be found.

In both of our cases, roentgen examination revealed the antra to be underdeveloped, with only a very small area of aereation superomedially in each. Contrary to the reports of obliterative frontal sinusitis and other acquired osseous lesions, no bony margins of an adult maxillary sinus could be outlined in our cases. Roentgen examination of our cases also revealed similar changes in the ethmoid labyrinths, and the frontal and sphenoid cells were likewise underdeveloped. In both of our cases, the condition was bilateral. There was no clinical or x-ray evidence of generalized osseous disease. Clinically, there was no evidence of infection of the sinuses at the time of examination, and a past history of repeated sinusitis could not be established in either case. Upon operation, in both cases, the anterior wall was composed of a hard and thick type of cancellous bone, and there was a dense diploic and sclerotic type of bone where the antral cavity should have been. No mucous membrane could be found in this bone. Therefore we feel that both of these cases of osseous obliteration of the maxillary sinus are developmental in origin. Figure 4 demonstrates osseous obliteration of a maxillary sinus following a radical antrostomy with vigorous curettement of the antral walls.*

It is felt that the term "sclerosis of the antrum" may be applied to these cases of developmental osseous obliteration of the antrum since there is actually a sclerotic or diploic type of bone present instead of an antral cavity. The authors do not have any evidence to support or disprove the Wittmaack theory as applied to the pneumatization of the accessory nasal sinuses. It is felt that some unknown factors in early life (infection, allergy, endocrine imbalance, trauma or what-not) influence sinus pneumatization. The failure of development of the paranasal sinuses is probably due to many different factors, and is not due entirely to neglected sinusitis in infancy, as the proponents of the Wittmaack theory would have us believe. This influence, whatever the cause, is manifest more often by inequality or aplasia of the frontal sinuses, but its effects are also seen in the maxillary sinus.

In summary, we believe the following conditions may be responsible for sclerosis of the maxillary sinus:

a. Acute or chronic inflammation of the mucosa of the antrum during the process of growth.

b. Disturbed endocrine function, especially of the pituitary, during the period of growth of the antrum.

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*The authors wish to acknowledge the assistance rendered by Dr. Howard H. Ashbury in studying the x-ray films, and in supplying the film shown in Figure 4.

c. Hereditary factors influencing growth and development of the skull, facial bones and sinuses.

d. Trauma at birth or in infancy with disturbance of the growth of the alveolus.

SUMMARY

1. The acquired conditions which may lead to osseous obliteration of the antrum are reviewed.

2. The term "Sclerosis of the Antrum" is proposed for osseous maldevelopment of the antrum.

3. Two cases of "Sclerosis of the Antrum" are presented.

4. The probable causes of this condition are enumerated, and a differential diagnosis is offered betwen this condition and the acquired conditions effecting osseous obliteration of the antrum.

5. It is felt that an "antrum" should not be created in these cases, when the condition is recognized.

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VI

THE GELATINOUS SUBSTANCE OF THE MACULA NEGLECTA

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In studies on the nature and function of the gelatinous substance covering the labyrinthine sensory epithelia, also the cupula maculae neglectae has been investigated, as will be reported here.

Macula neglecta is a sensory epithelium occurring constantly in the labyrinths in all the vertebrate classes including the Mammalia. (Alexander, 1905)

The sensory epithelium is somewhat variable in size and location, but on the whole it may be said to be located on the border between the superior and inferior parts of the labyrinth and to be innervated constantly from the inferior branch of the vestibular nerve. As emphasized by deBurlet, the macula neglecta is always "oriented" against the endolymph, and may be assumed to receive its adequate stimulation through the endolymph. As yet, its function is quite obscure.

The macula neglecta has been examined by many investigators. It was demonstrated first by Deiters in 1862 and since investigated, among others, by Benjamins, Retzius, Okajima and the Sarasin brothers. In a comprehensive review, deBurlet (1929) sums up our present knowledge concerning this structure; and the reader is referred to this review for detailed problems concerning the anatomical location, variation, occurrence, etc., of this sensory epithelium.

It was long assumed that macula neglecta as a detached part of the original macula communis possessed a gelatinous substance of similar character as the gelatinous substances observed on the cristae and maculae and over the organ of Conti. This gelatinous substance has been observed by several authors without it being settled for sure whether it belonged to the tectorial-like or cupula-like type—i.e.,

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being attached only to the sensory epithelium, with the cells of which it is connected—or whether it was attached also elsewhere in the region. Otoliths have never been seen in the gelatinous substance.

The details in the nature of this gelatinous substance are rather unknown, and studies on this question meet with the same difficulties as other studies on similar gelatinous structures. With the experimental animal employed by the writer—spiny dogfish (Acanthias vulgaris)—these difficulties have proved somewhat less than expected, so that it has been possible to recognize at least some of the characteristics of this substance without resorting to the Altmann-Gersh freezing-drying method. In practice this otherwise highly serviceable and desirable method implies some difficulties concerning animals which are caught far away from institutes where the technical material required for this method is available.

MATERIAL AND TECHNIQUE

The studies here reported were carried out on a considerable number of adult sharks, partly in vivo, partly immediately after they were killed, and, finally—especially in the introductory studies—on sharks that had been dead for about one day.

The histological sections originate from adult sharks, fixed in vivo in two different ways. On several sharks the Wittmaack fixation fluid was injected transcardially into the aorta. After trimming and dissection of the cranium, this was placed in the same kind of fixation fluid. As this method did not always give optimal fixation, in the remaining sharks an opening was made into the perilymphatic space round the lateral semicircular canal in vivo and a very fine glass capillary was cautiously introduced into this space, and through this capillary the proximal part of the perilymphatic space was perfused with formalin-mercuric chloride or with Bouin's fluid. The fixation after the latter method was satisfactory. Immediately after this the cranium was dissected free and then placed in the fixation fluid after an opening was made into the perilymphatic space surrounding the remaining two semicircular canals.

All the specimens were embedded in paraffin and cut in sections of 10 μ. The following staining methods have been used: hematoxylin eosin, hematoxylin-mucin, hematoxylin-carmine, gallocyanin chrome alum (after Einarson), and toluidine blue.

ANATOMICAL FEATURES OF THE SHARK LABYRINTH

As the anatomical aspects of the macula neglecta in the elasmobranchii present some peculiar features, it will be appropriate here briefly to mention them.

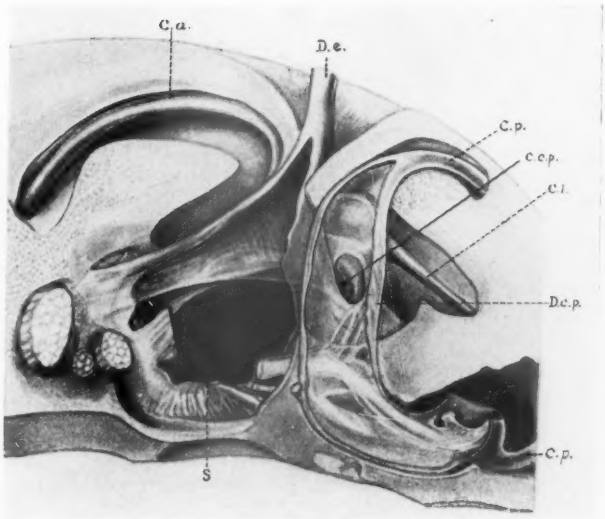

Fig. 1.—Labyrinth of acanthias, seen from the medial side. Medial wall of the sacculus removed. Ductus canalis semicircularis posterior opened by excision of its medial wall. Canalis communis posterior is seen as well as the posterior branch of the acoustic nerve and the ramus maculae neglectae. Drawn from writer's dissection.

c.a.—canalis semicircularis anterior; *c.l.*—canalis semicircularis lateral; *c.p.*—canalis semicircularis posterior; *d.c.p.*—ductus canalis semicircularis posterior; *U*—utriculus; *R.U.*—Utricular recess; S.—sacculus; *D.E.*—endolymphatic duct.

In the shark the posterior semicircular canal forms an annular tube, as that section of the utriculus which was to supplement the ring formation commenced by the posterior semicircular canal in these animals is detached from the rest of the utriculus. This section—which Stewart designates as the "posterior utriculus"—forms a perpendicular, wide, thin-walled tube, connecting the two limbs of this semicircular canal (Fig. 1). This tube will here be designated by the non-committal term "ductus canalis semicircularis posterior" ("d.c.s.p.").

The resulting closed ring formation is connected with the rest of the membranous system of the labyrinth through one communication: a membranous tube, the dimensions of which vary in the different species of elasmobranchii, running from the utricular section

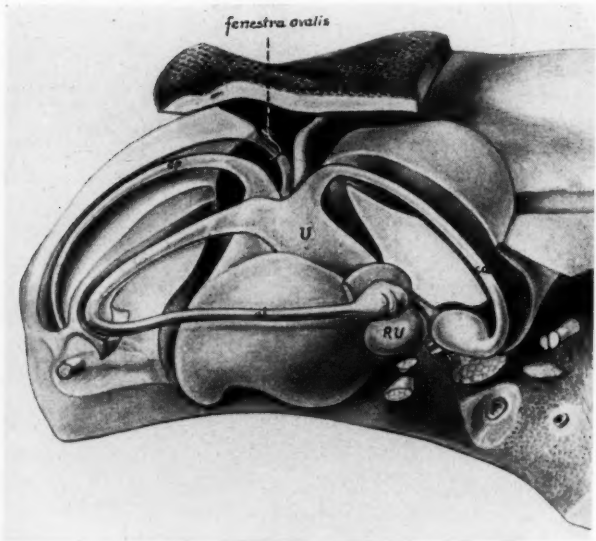

Fig. 2.—Labyrinth of acanthias, seen from the lateral side. Note upper part of the ductus canalis semicircularis posterior and its transition into the canalis semicircularis posterior; also the fenestra in the cartilage at this site. Fenestra closed by the membrana fenestra ovalis.

c.a.—canalis semicircularis anterior; *c.l.*—canalis semicircularis lateral; *c.p.*—canalis semicircularis posterior; *d.c.p.*—ductus canalis semicircularis posterior; *U.*—utriculus; *R.U.*—Utricular recess; *S.*—sacculus; *D.E.*—endolymphatic duct.

of the ring downwards, laterally and forwards to the sacculus, into which it opens. As is evident from Fig. 1, this inlet is located on the posterior medial aspect of the sacculus, posteriorly to the departure of the endolymphatic duct. The communicating tube between the ring of the posterior semicircular canal and the sacculus will here be designated as the "canalis communicans posterior" ("c.c.p.").

The *macula neglecta* is located as an epithelial thickening in the wall of the canalis communicans post., and it is seen to cover a section of the entire wall of this canal with exception of a narrow zone anteriorly, on which account it has to be described in the shark as being nearly cylindrical.

Topographically, the macula presents two features of particular interest:

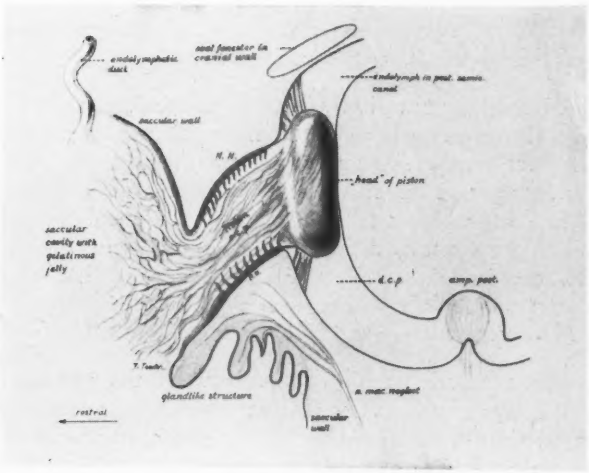

Fig. 3.—Schematic drawing of the described topography of the macula neglecta. Note "piston" and "head of piston." *D.c.p.*—ductus canalis semicircularis posterior. *M.N.*—macula neglecta with "cilia-like" tufts projecting into the gelatinous "piston." Note also the tectoria-like attachment of the "head of piston" to the walls of the ductus can. post.

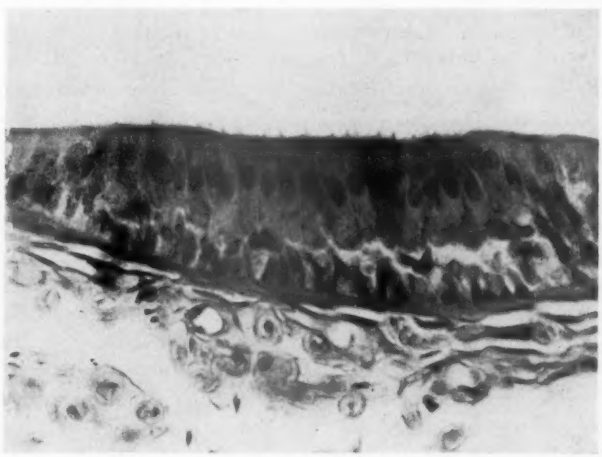

Fig. 4.—Part of macula neglecta showing sensory cells and "cilia." Magnif. x 400. Hematoxylin-eosin.

1. It is located in the wall of a tube that establishes the only passable connections between the posterior semicircular canal ring and the rest of the labyrinth.

2. It is located immediately beneath an opening in the cranium (Fig. 2). This opening is an oval fenestra that connects the subcutaneous tissue on the dorsum cranii with the perilymphatic space round the d.c.s.p. and the crus simplex of the posterior semicircular canal. The fenestra is closed by a thin, elastic membrane of connective tissue (it is readily depressed, for instance, with a probe, and then it resumes its original form and appearance). This fenestra is the *only part of the labyrinthine wall capable of yielding to variations of the external pressure.*

The shark travels at all depths between the surface and a depth of 400 m or more. As its endolymphatic duct opens on the skin of the back, thus connecting the labyrinthine cavity with the surrounding water, it is reasonable to assume that variations in the pressure round the animal to some extent may be transmitted to the endolymph through the endolymphatic duct. In this way the pressure variations are transmitted to the cav. sacculi and further on. The transmission to the posterior voluminous semicircular canal section may take place only through the c.c.p. and thus through the cylindrical tunnel of sensory epithelium on the walls of this canal.

Balancing of the variations in pressure may be expected in some degree to be practicable also through the fenestra ovalis, but the anatomical conditions make it rather unreasonable to think that the variations in pressure from the cav. sacculi may be completely balanced in this way.

OBSERVATIONS

The endolymphatic space over the tunnel-shaped macula neglecta is quite filled with gelatinous masses. Also the sacculus proves to be filled with a gelatinous mass instead of the watery endolymph characteristic of the anterior and lateral semicircular canals and also of the ring of the posterior semicircular canal. The gelatinous mass of the sacculus becomes more condensed at the departure of the can. communicans post. and continues through this canal, filling it completely. The gelatinous substance in the canal is considerably more tenacious and more viscous than the substance in the sacculus, and on following the gelatinous mass further back it is seen to expand spherically at this inlet into the wide ductus canalis semicircularis posterior. This expansion is the end of the gelatinous mass, which here forms a large semispherical prominence of jelly that occupies

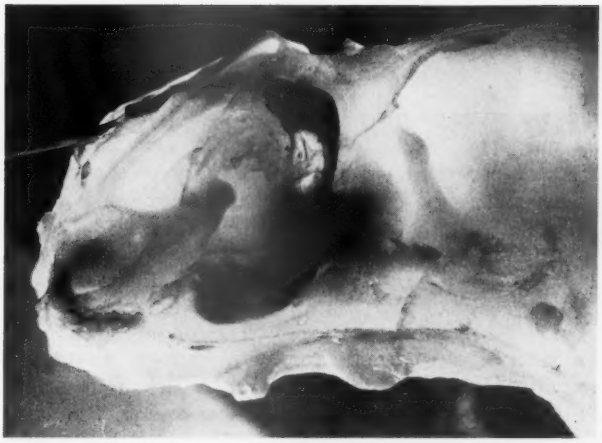

Fig. 5.—Left half of the cranium, seen from the medial side. Ductus canalis semicircularis posterior laid free, and India ink injected through the can. semicircularis post. at the needle to the left. The negative picture of the piston head is seen. The dark field to the right of (in front of) the ductus is due to impression by an India ink-stained finger.

Fig. 6.—Same preparation as Fig. 5—1 hour later. Now the preparation had dried, and the ductus was cut open. Canalis communis posterior is seen to depart from the bottom of the ductus, and a little India ink is seen below in the canal. Both Fig. 5 and Fig. 6 are photographed by transillumination. In Fig. 6 the preparation is tilted less around its longitudinal axis than in Fig. 5.

a part of the lumen in the ductus canalis semicircularis posterior. Thus the jelly here assumes the form of a mushroom, the "cap" of which is formed by the expansion, the "stalk" by the contents of the canal.

If this structure is supposed to be quite immobile, it may hardly serve any purpose. We therefore have to assume that the "mushroom" is capable of at least very slight motion—presumably mere shifts, under which the cylindrical "stalk" moves like a piston in the longitudinal direction of the canal. Thus the sensory "hairs" on the macula neglecta (Fig. 4) will be deflected, giving rise to the impulse that has to be looked upon as adequate to the demands on the labyrinthine sensory organs.

Such motions of the jelly in the can. communicans posterior, however, will necessarily be accompanied by simultaneous and corresponding movements of the hemispherical prominence at the end of the "piston" with resulting changes in the contents of the posterior semicircular ring.

The above considerations are based on the following observations:

1. When the sacculus is opened on a living shark, its contents are seen to be viscous and stringy. Owing to their consistency, the contents may be withdrawn with a wide hypodermic needle only with great difficulty. This endolymphatic jelly keeps the walls of the sacculus slightly distended, and, because of the "elasticity" of the walls, the jelly is forced out through an artefact opening, forming soon a little "misty veil" over the hole in the saccular wall. If the preparation of the specimen is performed under water, the"veil" is seen slowly to increase, while at the same time the sacculus collapses.

2. If the ductus canalis semicircularis posterior in a newly killed shark is dissected so free as to give a good view of its entire course, the opening of the can. commun. post. is seen distinctly. But the above-mentioned gelatinous structure cannot be made out on direct inspection. It can be rendered visible, however, by injection of dilute India ink into the upper section of the posterior semicircular canal (Fig. 5 and 6). Now the India ink can be followed from the site of the injection in the crus simplex, and from here farther downwards through the ductus can. semic. post. towards the ampulla posterior. The India ink is clearly seen to stop at the inlet of the canalis communis posterior. The broad column of India ink is trying to make its way farther downwards, and it is seen to continue as two filmy veils, anteriorly and posteriorly along the walls of the canal, while the central part of the lumen is not stained

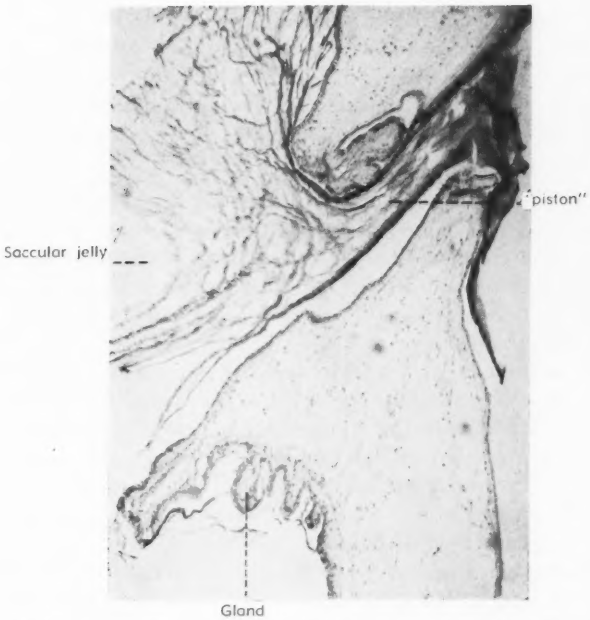

Fig. 7.—Canalis communicans laid open by incision along its axis near the posterior wall of the canal (on which account it seems narrow). Note saccular jelly and its transition into the "piston." The "piston head" is distorted in this section. A part of the gland-like formation is seen below. Gallocyanine chrome-alum.

Fig. 8.—Transversal section parallel to—and behind—the course of canalis communicans posterior. Saccular jelly and "head of piston" are well seen. This shows that even after alcohol treatment this head is considerably larger than the orificium of the canalis communicans posterior. Gallocyanine chrome-alum. x 100. All sections in this region are torn due to the nearby saccular otoliths.

with India ink. Below the inlet of the communicating canal the two thin streaks of India ink unite into one whole that completely fills the rest of the canal, down to the posterior ampulla. In this way a clear negative picture is obtained of the hemispherical gelatinous structure that is seen almost to fill the lumen of the ductus canalis semicircularis posterior its convexity aiming upwards and backwards.

3. When in such a specimen the intrasaccular pressure is increased by means of injection through a hyperdermic needle introduced into the endolymphatic duct, the India ink column in the posterior semicircular canal will be seen to move backwards in relation to the site of injection. In this way it is easy to obtain a shift of the India ink column amounting to 2-3 mm, and this shift is reversible, as the end of the India ink column returns to its initial position after the artificial endosaccular overpressure has ceased. On well injected specimens the movements of the "gelatinous hemisphere" are visible on direct inspection, and an intrasaccular overpressure is seen to shift the hemisphere backwards and upwards, i.e., in the direction of the site of departure of the crus simplex. Thus relatively large amounts of fluid are set amoving in the wide ductus canalis semicircularis posterior and when it is forced into the narrow semicircular canal a not inconsiderable shift of fluid takes place in this canal.

4. On hardening of a freshly removed shark labyrinth in alcohol, the gelatinous substance becomes more tenacious and now, by means of pincers it can be pulled out in one piece, and this pulls along also the "piston" in the canalis communis posterior and its "head"—all in one piece. This clearly indicates an intimate structural connection with the rest of the saccular contents. In such an alcohol-hardened specimen the gelatinous hemisphere is directly visible to the naked eye after opening of the ductus canalis posterior, even though it now has shrunk considerably because of the water-absorbing capacity of the alcohol.

The structure of the saccular jelly and its continuation through the canalis communis posterior is also seen clearly in histological sections where the jelly appears as a reticular formation of quite definite architectural structure encountered in all the specimens, regardless of their preceding treatment, staining, etc. (Fig. 7-8). This network stains well and is quite conspicuous in sections stained with hematoxylin as well as with gallocyanin chrome alum. The latter staining method brings the outline out in black, and here the staining is very intense. With toluidine blue the jelly stains metachromatically reddish-violet—like cartilage—and thus presumably it

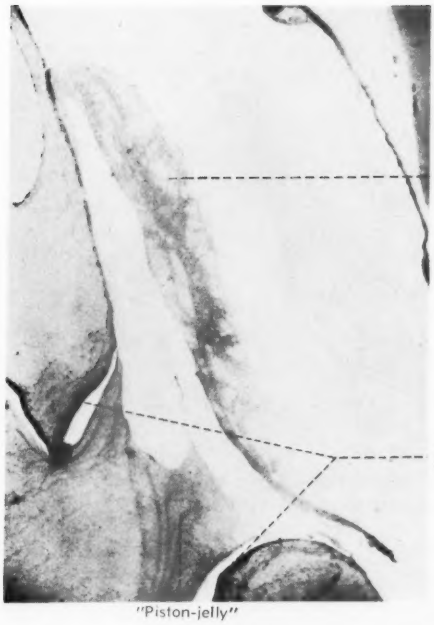

Fig. 9.—Transversal section through the middle of canalis communicans post. Macula neglecta is seen on the upper and lower walls of the canal. Poorly stained remnants of the "piston jelly" are seen together with the (shrunken) head of the piston. Note fixation of the head of piston which is seen above (in the ductus canalis semicircularis posterior.) Hematoxylin-eosin. x 40

discloses a content of mucous substance. This structure may be observed also in unstained paraffined section on microincinerations and in similar sections under the phase contrast microscope (it is always somewhat torn due to the nearby chisel-containing saccular otoliths).

Without here entering into the structural details of the saccular network, it is to be mentioned that at the departure of the can. commun. post. all the fibrils are gathered into mostly parallel close-packed bundles (Fig. 7), which quite fill the canal and extend to the hemispherical prominence. The hemispherical prominence into the ductus can. semicircul. post. is seen in the sections (Fig. 9 and 10) to be stamped by shrinkage, making it difficult to say anything definite about its structure. It seems not to be characterized by its presumably fibrillary content to such an extent as might be

Fig. 10.—Enlargement of upper attachment of "piston-head" to the wall of ductus canalis semicircularis posterior. x 200

expected. Under relatively low power—(up to a linear magnification of 250)—no definite fibrillary structure can be made out. On higher magnification, and especially in gallocyanin-stained sections, this mass rather looks as if it consists of close-packed bundles of very delicate fibrils, the bundles being conglutinated by amorphous interfibrillary substance.

In the sections the "hemisphere" is seen to be attached to the walls in the ductus can. semicirc. post. by long thin strands, presumably elastic (Fig. 10). This prominence appears to be very resistant. In many sections it is seen to have become detached from its "anchorage," overlapping the rest of the section in a haphazard way. But also in such cases it has always preserved the same form and appearance as in the sections presenting it *in situ*.

Making full allowance for the possibility of artefacts being produced in the handling of the specimens, the presence of the hemispherical gelatinous formation here described and its "stalk" may be looked upon as established. The microscopic structure here observed may possibly be artificial but its uniform appearance, pronounced stainability and expedient architecture still speak in favor of its actual existence.

From the above, then, it seems reasonable to take for granted that the substance over the macula neglecta is made up of a

gelatinous structure that covers the entire sensory epithelium of the macula, and which is in part attached outside the macula itself. The cells of the macula are seen to be equipped with "cilia"* (Fig. 4), and these may reasonably be assumed to extend into the jelly in the can. commun. post.

Before appraising the above findings, however, a few more anatomical details are to be mentioned.

In the first place, the wall of the sacculus round the anterior inlet of the canalis communicans is changed to the extent that the normal low cuboidal cells lining the wall have been replaced by *secretory epithelium*. This epithelium—which is described in another work—appears in part as a high columnar epithelium with noticeable droplets of secretion in its luminal part. These droplets may be followed through all stages of the secretion and they are seen also as free droplets in the lumen. In sections stained with hematoxylin and Best's carmine the droplets are red in color and may thus be assumed to contain glycogen. This secretory epithelium is chiefly found dorsally to the inlet of the can. commun., though also laterally to this.

The secretory epithelium, however, presents itself also in a different way. Ventrally to the inlet of the can. commun. we thus find the epithelium protruding into the lumen, and here the surface is irregular and jagged (Fig. 6), with small villous-like projections. This results in a gland-like mass, the inner part of which is made up of numerous tiny vessels, and which is covered by a low columnar epithelium. Secretory droplets have not been demonstrated here, and the assumption of the epithelium being secretory is based chiefly on its resemblance to secretory epithelia elsewhere. The first-mentioned epithelium is innervated by the ramulus maculae neglectae, whereas the innervation of the other epithelium is unsettled yet. Still, it seems rather likely that also this epithelium is innervated from the same source as the first-mentioned.

In the next place, it is to be mentioned that whenever the macula neglecta has been described it was localized to the border zone between the utriculus and sacculus, from which it may extend for a varying distance on the walls of the two membranous sacs. Anatomically, histologically and physiologically these two sections of the labyrinth are widely different, and it is a characteristic feature that this sensory epithelium everywhere is localized to the border zone between the two sacs.

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*Probably cytoplasmic extensions from the cells of the macula.

If, with our present knowledge, we try to form some idea about the function of the macula neglecta, it must be kept in mind that its location makes this structure inaccessible to direct physiological intervention, and, as it cannot be isolated, our interferences will have to be based entirely on the established anatomic and histological data.

Even though structure and function are inseparably united, it cannot be taken for granted that the latter may be read from the former. It is a sure thing, however, that knowledge of the anatomical structure of a given part is a sine qua non to the understanding of its physiological aspects, and as long as the latter are obscure, this knowledge may furnish some valuable evidence to be utilized in further physiological investigations.

In order to facilitate the survey of the established data it will be appropriate here briefly to summarize them:

a. The sensory epithelium is always located on the border between a static and a (presumably) acoustic system. The two systems have different connections with the surroundings of the labyrinth; in acanthias their fluid contents differ in character—and this may perhaps be encountered in other animals too (thus the author has demonstrated this in cod).

b. The covering substance of the macula neglecta connects the contents of the two systems with each other and also with the sensory cells of the macula neglecta. Any difference of pressure in the two systems will directly act upon the sensory cells of the macula; and acoustic vibrations in one system that are not accompanied by identical vibrations in the other system may likewise act upon the sensory cells of the macula.

c. In acanthias we find a special mechanism through which pressure variations in the pars inferior (for instance, from diving, secretion or vibration) readily are transferred to the pars superior ("utriculus post." and ampulla post.) bringing about just those changes which adequately stimulate the cells of the macula itself (deflection of the cilia).

Parallel mechanisms are unknown in other vertebrae classes, which—as far as I have been able to find out—have not been examined with reference to this point.

Pressure variations arise more easily in the pars inferior than in pars superior because the endolymphatic duct connects the cavity of the sacculus with the surrounding water and may thus transmit the

variation of pressure (up to several atmospheres) to the pars inferior. Furthermore, secretory epithelia are rare in the pars superior.

DISCUSSION

If, in conformity with Lowenstein and Roberts* (1949), we assume the macula neglecta to be a part of the acoustic mechanism, the following features may conceivably speak in favor of this view:

a. The macula neglecta is located in the lower part of the labyrinth that otherwise appears in acanthias not to have a vestibular function. As to the sacculus lagena function in acanthias, we know from experiments performed by Parker and by the writer that it seems to be able to function as a sound-perceiving apparatus.

b. It is innervated by the inferior branch of the acoustic nerve, together with the sensory epithelia of the above-mentioned membranous sacs.

c. Acoustic vibrations in the saccular jelly may hardly avoid stimulating the macular cells, while it is difficult to imagine that a change in the posture of the head may stimulate these cells.

d. The macula neglecta is located in immediate relation to the perilymphatic fenestra which may catch and counter-balance the vibrations of the covering substance of the sensory epithelium transmitted from the saccular jelly.

e. Electrical responses in nervous maculae neglectae (Raia Clavata) are recorded by *acoustic* stimulation, but not by spatial change of head position (Lowenstein and Roberts, 1949). Contrary to Selachians, this nerve is accessible in rajidae.

The alternative possibility appears to be that for adequate stimulation the macula depends on pressure differences of another character between the two sections of the labyrinth. The peculiar hemispherical "head of piston" and its location are difficult to interpret. Probably any movement of the macularium (the piston) is accompanied by corresponding movement of the "hemisphere;" and very likely these movements will be transmitted to the endolymph in the section of the pars superior here concerned—and in this we find the posterior ampulla with its sensory epithelium, which may hardly be imagined to remain quite unaffected by such vibrations.

The study of this particular gelatinous substance is interesting because in several ways it throws some light on the nature of the

*Already Breuer assumes that M-N serves acoustic functions in fishes. Later investigators (e.g. Okajima III and Gaupp) subscribe to this view.

other gelatinous substances. To a large extent their structure and mode of function are still unexplored. As it is reasonable to assume that all these gelatinous masses in their fundamental structure present some points of great resemblance, it is to be hoped that detailed information about the nature of this particular gelatinous substance ultimately may contribute also to solve some of the problems involved by the other gelatinous substances.

Also the function of the labyrinthine sensory epithelia is still very obscure as to its details. Hence we have to make use of any way by which we may enter further into this problem, and one of these ways, the writer thinks is to investigate the character of the "trigger mechanism" required for the production of the adequate stimulation of the sensory cells. There can hardly be any doubt that just the character of the "trigger mechanism" may become obvious from the complete picture of the structure of the gelatinous substances, their precise location, attachment, etc.

SUMMARY

The gelatinous substance of the macula neglecta is made up of a tenacious, viscous mass which in sections shows a uniformly fibrillary structure. Its building-up appears to be determined by the topographical conditions as the gelatinous substance consists in a cylindrical mass that on one side connects with a similar gelatinous mass in the cavum sacculi, whereas on the other side it ends in a semispherical prominence that partly fills the lumen in a zone of the posterior semicircular canal.

An account is given of the findings rendering this architecture probable, and the conceivable physiological consequences of this in connection with certain anatomical features are discussed.

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VII

A DISCUSSION OF THE COMMON TYPES OF CHRONIC RHINITIS

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Chiefly because of recent advances in chemotherapy and the use of the antibiotics, the time has come when an absorbing interest in acute infections of the ear, mastoid and sinuses can no longer push to the rear an equal interest in diseases of the nasal mucous membrane. The symptoms of chronic rhinitis are not dramatic, the signs often not obvious, the treatment seldom clear and sure. Nevertheless, the frequency of its occurrence and the degree of discomfort it causes, demand that we give this group of disorders their due thought and study. Only by such well directed effort can we improve our accuracy of diagnosis and the treatment of these common afflictions.

In this paper I shall attempt to discuss five definite types. These are: 1) Chronic bacterial, 2) Simple catarrhal or intumescent, 3) Hypertrophic, 4) Hyperplastic and 5) Atrophic. A consideration of vasomotor disorders and of neoplastic and specific disease will be omitted.

CHRONIC BACTERIAL RHINITIS

Subacute or chronic bacterial rhinitis is seen both sporadically and in the epidemic form. In my experience it is most frequently, but not invariably, a complication of a severe upper respiratory infection. Whether it will appear or not seems to depend on the virulence of initial invader and the resistence of the host. The condition can occur without preceding acute infection, but in such cases the patient is almost invariably already debilitated with fatigue or some general disorder.

It is my opinion that what occurs here is as follows: the continuity of the mucus sheet, ciliary action and other necessary factors in normal nasal function are interrupted by the acute infection. Either because of the virulence of the invading organism or because of a lack of resistance of the host, or both, prompt return to normal nasal function does not occur. This allows the secondary bacterial invaders to remain unmolested. Repeated cultures in a large num-

ber of cases have revealed staphylococcus aureus in every instance. The organism is usually hemolytic and highly toxic as demonstrated by the coagulase test.[3-10]

The signs are quite characteristic. The nares are usually coated with dry purulent crusts. The mucous membranes throughout are bright red, denoting arterial dilatation rather than venous congestion. Scattered over the membranes are isolated purulent crusts that in my opinion represent breaks in the continuity of the mucous blanket. Strangely the nasal airway is usually good with only a minimum of edema of the turbinates. On the floor of both nostrils is commonly a pool of thick tenacious mucus. This same material is often seen covering the nasopharynx, pharynx and larynx. These structures appear injected secondary to the infectious postnasal drainage. Anatomical variants such as a deviated septum, do not seem to be important factors in the etiology of this condition.

Patients suffering from this type of rhinitis complain chiefly of a dry stuffy nose, a useless nonproductive cough, and lassitude. Other symptoms encountered are frontal headache, pain over the bridge of the nose, postnasal discharge and burning of the eyes. A bilateral or unilateral conjunctivitis is a frequent complication of this disease. Furthermore, in a high percentage of cases the organism recovered from the eye is the same as that found in the nose.[3]

Treatment should be directed towards eliminating the offending organism, thereby promoting the return of normal nasal function. In my experience a solution of penicillin used as nose drops is the best. According to work done by Proetz, a concentration of 2000 units per cc is adequate and not injurious to ciliary activity. Decongestants are definitely contraindicated. In the first place there is seldom any marked turbinal swelling, and in the second place enlarging the airway tends to increase the tenaciousness of the mucus which is already too sticky and thick for normal function. For the latter reason, I feel that solutions of penicillin rather than powders are much preferred. Further therapy should be directed towards building up the patient's general resistance. This condition untreated can last for weeks or months, but in my experience responds well to the simple measures outlined above.

SIMPLE CATARRHAL RHINITIS

Simple catarrhal or intumescent rhinitis is a definite entity and one that is often extremely difficult to cure. The causes of this disease can be conveniently divided into two main groups; those pertaining to conditions in the nose itself, and those involving gen-

eral physical and emotional factors. There is no question that long-standing though perhaps minimal derangements in nasal physiology produced by deviated septum, nasal polyps, hypertrophied turbinates and other sources of partial or complete obstruction will bring about this condition. Other causes which must be included in the group working in the nose itself are environmental. By these we refer to exposure to irritating dusts and vapors, the influence of tobacco smoke, the effects of poor winter and summer air conditioning, and last but by no means least the prolonged use of any intranasal medication. The otolaryngologist should never fail to consider the body as a whole when searching for the etiology of a chronic rhinitis.

That simple catarrhal rhinitis is frequently a manifestation of general lowered resistance cannot be denied. Common factors favoring the development of this condition are long-standing fatigue, exhausting febrile diseases such as a severe upper respiratory infection or pneumonia. Pronounced debilitation from heart disease, arthritis, diabetes mellitus, tuberculosis, the various nephritides, blood dyscrasias, carcinomatosis, and other serious illnesses must be considered. The role that diet plays in this type of rhinitis is not entirely clear to me. I am convinced that vitamin deficiency, especially vitamin A, is an important factor. Less convincing to me is the commonly mentioned role of carbohydrate and starch consumption. In this regard it seems likely that a poorly balanced diet is not so vital as far as nasal physiology itself goes, but is most important from the standpoint of improving the general physical condition. Endocrine disturbances must not be overlooked. Without question hypothyroidism heads the list as far as the rhinologist is concerned. Perhaps the most recent group of conditions now recognized as an important cause for intumescent rhinitis is that involving the central nervous system. It seems less remote that such disorders are capable of bringing about a rhinitis when we consider that an intumescent congestion of the nasal mucosa is fundamentally a derangement in the neurovascular mechanism. It is not uncommon, therefore, to see this condition complicating various mental and emotional states. Perhaps most important in this group are prolonged states of tension and anxiety.[12]

The better understanding of any disease includes a knowledge of the pathology. Like all other parts of the respiratory tract it is the dynamics of nasal pathology that concern us most. In other words, it is pathology expressed in terms of altered physiology that gives us the best clue to the disease under consideration. This is obviously apparent after a careful contemplation of nasal physiology. The relatively recent advances in this science have had far reaching

effects on nasal therapy, not only surgical, but conservative management as well. For this happy state of affairs we are everlastingly indebted to Proetz. His contribution to our present knowledge of nasal and sinus physiology is monumental. As stated above, the underlying pathology in simple catarrhal rhinitis is an upset in the neurovascular control. Here the delicate balance that maintains the correct patency of the deeper radial arteries and veins is lost. Thus these vessels are in a constant state of dilatation. This explains the increased diameter of the turbinates, especially the inferior. It will be noted that the turbinates are not strictly edematous, but enlarged due to deep vascular dilatation. It is for this reason that with a probe one can demonstrate soft swelling, but when the probe is removed from the inferior turbinate there is no pitting. With these vascular changes in the deeper layers there is no concomitant dilatation of the superficial group of arteries and veins. Therefore, one does not expect to see a hyperemic membrane in this condition. Characteristic of this type of rhinitis is also an increase in the viscosity and the amount of mucus produced. With these changes having taken place, it is obvious at once that nasal physiology is now grossly disturbed and will not return to normal until these underlying factors have been corrected. One of the functions of the nose is to keep itself in order. Now that the normal physiology is upset, it can no longer do this. It is my contention therefore, that a nose so affected by an intumescent rhinitis immediately becomes the site of multiplying toxic bacteria. Repeated cultures have shown, as in the case of the bacterial rhinitis, toxic staphylococcus aureus. It is also my belief that any attempts to correct the underlying upset sympathetic control of the nose will fail as long as secondary bacterial infection is allowed to persist.

This condition is characterized by shifting stuffiness. The nasal congestion is also noticeably worse at night. Patients will often state that as they lie in bed, the upper nostril is invariably the clear one. It seems that position definitely plays a role in the degree and site of congestion. Upon awakening in the morning, there is a large amount of thick clear mucus present in nose and larynx. This gives rise to much ineffective nose blowing and clearing of the throat which rather than helping matters only tends to increase the congestion and discomfort. The profuse postnasal discharge frequently gives rise to a secondary pharyngitis and laryngitis. These are quite constantly worse in the morning upon awakening and again in the evening. Nocturnal useless coughing is a frequent complaint of those suffering from this illness. Commonly these patients complain of pain over both antra often simulating that of acute antritis. At

other times there is dull frontal headache and pain over the bridge of the nose. Secondary eustachian tube involvement and conjunctivitis is common. Anosmia is not usually seen since the middle turbinate is customarily not involved to the extent of the inferior, and, therefore, does not block the highest stream of inspired air en route to the olfactory area. The most exasperating symptom from the standpoint of the patient is perhaps the occurrence of repeated acute exacerbations. Frequently after exposure to some irritating dust or vapors, or for no apparent reason at all, the patient will experience an intense tickling in the nose followed by several violent sneezes. A copious flow of watery mucus will ensue followed by a great increase in the amount of nasal stuffiness. After several hours or days this will subside only to recur. Often but not invariably, there is seen pronounced lassitude, easy fatigability, and various degrees of mental depression. In general it can be said that patients suffering from this illness are genuinely miserable and have just reason to expect thoughtful energetic care.

Nasal examination reveals quite characteristic findings. The membranes are usually of normal color, but sometimes moderately hyperemic. The most important sign is the presence of so-called pillow edema. This is elicited by pressing the inferior turbinate with some suitable instrument and observing how readily an indentation is made. Upon removal of the pressure, the indentation quickly disappears. As brought out above, this is not true edema at all, but rather increased size of the turbinate by vasodilatation alone. As pointed out by Proetz, the mucus blanket is invisible in a normally functioning nose. In this condition, on the other hand, strands of mucus extending from the inferior turbinate to the septum and small pools of clear mucus lying on the floor of each nostril are almost the rule. Unlike the bacterial rhinitis mentioned before, areas of superficial ulceration with interuptions in the mucous blanket are not apparent here. Instead patches of accumulated mucus are frequently seen lying over the inferior turbinate, the septum and the inferior border of the middle turbinate. Perhaps one of the most striking signs in simple catarrhal rhinitis is the dramatic reaction to any applied decongestant. A spray of a very small amount of neosynephrin ¼% or ephedrine 3% will produce exceedingly rapid and pronounced results. This is not surprising when we consider that this condition is essentially one of neurovascular dysfunction. Commonly, as might be expected, one finds a deviated septum, polyps, hypertrophied turbinates and other causes of chronic nasal block. In this regard it seems wise to emphasize the importance of nasopharyngeal examination in these cases. Since nasopharyngeal tu-

mors, both benign and malignant, are reasonable causes for long-standing nasal block, it is not surprising that an intumescent rhinitis is often a helpful lead by way of discovering these very important lesions.

Treatment should be successful if carried out with the underlying general and local pathology in mind. It goes without saying that any general physical disorder must be corrected before improvement may be expected. For this reason it would seem a sound idea to insist on a general medical checkup in every case. If a definite psychiatric factor is present the proper disposition will depend on the severity of the condition. Superficial emotional states can be expected to frequently resolve with the improvement of some environmental situation alone, more profound alterations from the normal will definitely require psychotherapy. No improvement can be anticipated if these personality factors are allowed to continue. In general it may be said that local therapy should be directed to encouraging the return of normal nasal physiology. In my experience the most important step toward this end is to rid the nose of the invariably present secondary bacterial infection. In all cases cultured this has almost always been a highly penicillin-sensitive strain of toxic staphylacoccus aureus. Penicillin nose drops, in a strength of 2000 units per cc, has been very effective. This alone has, in a number of instances, been sufficient to clear the condition. More often further steps are necessary. High doses of vitamin A seems to be a very effective way in which to build up the mucous membrane. In the vicinity of 200,000 units a day works very well as an initial dose and then after the first week this can be reduced as the condition improves. In intumescent rhinitis the viscosity of the mucous is increased. Therefore, any therapy which inadvertently tends to further this abnormal viscosity will obviously aggravate the disease. The two most common errors in this regard are the use of decongestant nose drops and the use of various chemotherapeutic or antibiotic powders. In the first instance the airway is promptly increased and the resultant greater volume of air in the nose tends to produce drying which in turn increases the viscosity of the mucus already too thick to lend itself to normal function. The intranasal insufflation of powders will of course produce the same undesirable effects. Therefore, it is best to decongest the nose only in the office, where a thorough cleaning with tip suction is greatly enhanced by so doing. The use of solutions of neosynephrin, ephedrine or other constrictors should be limited to such times as the nasal stuffiness becomes unbearable, or just before bedtime to insure the patient a restful night. There is no indication at any time for the use of

colloidal preparations of silver and allied drugs, since these tend to put an additional load on the cilia which are already struggling to move the blanket of sticky thick mucus. It is obvious that such a disease of the nose can be the cause of a chronic conjunctivitis. It seems equally logical to me that a conjunctivitis can be a factor in perpetuating an intumescent rhinitis. In fact it has been my experience over and over again, that all the above treatment mentioned will be of no avail unless the patient is instructed to use a suitable eye wash. This I prefer to have them do with an eye cup, used with forceful winking in order to force the solution down the lacrimal duct. This procedure will often turn the tide in a recalcitrant case even though no obvious conjunctivitis is apparent. Surgical measures to correct anatomical variants within the nose are decidedly indicated in some cases. When possible it is best to postpone them until the particular episode is over. I refer to submucous resection, polypectomy, fracture of the turbinates, the removal of nasopharyngeal masses, etc. Other helpful measures are complete abstinence from alcohol, reduction to complete avoidance of tobacco, elimination of exposure to irritating vapors and additional rest. Several patients who have come under my care have tried the use of infra red rays. In every instance they were both subjectively and objectively worse than before. It is now routine for me to caution them about such practice including prolonged exposure to the sun.

Even if all sources of therapy are utilized, complete cure often takes from several days to several weeks and patients should be advised not to expect a dramatic recovery. Of course there are cases where all efforts fail, but these should be few provided the condition is treated early in its course.

HYPERTROPHIC RHINITIS

Hypertrophic rhinitis might well be considered as a complication of simple catarrhal rhinitis. It usually results from an intumescent rhinitis that, for one reason or another, has never resolved. It may also develop as a result of repeated acute infections of the nasal mucosa. Lowered resistance of the patient may also have to be considered.

The pathology in this type is quite different than in the former. With the long standing arterial and venal dilatation and the subsequent secondary infection found in the intumescent type, there gradually develops a perivenal and perlymphatic inflammatory reaction. This is characterized by a perivascular infiltration of lymphocytes and plasma cells chiefly. This peravascular cuffing continues until venous and lymphatic drainage are severely hampered by the

consequent constriction of these structures. With the arterial supply uninterrupted and return flow increasingly embarrassed, edema into the tunica of the nasal mucosa is to be expected. Thus the increased size of the turbinate in this type of rhinitis is due to true edema rather than vascular dilatation. This form of chronic rhinitis is further distinguished from the simple catarrhal type by the presence of venous congestion, rather than merely venous dilatation.

With such profound changes occurring in the tunica, the source of nutrition to the more superficial layers, it is apparent that changes may also be expected above. It is known by histological examination that there often ensues a metaplasia of the surface ciliated epithelium and a marked alteration in the activity of the mucous glands. It would seem reasonable to assume that earlier alterations would consist in slow ciliary activity and a pooling of old mucus in the glands themselves; the latter being brought about not only by the retarded motion of the cilia which help to carry mucus out of the glands, but also from the slow production of mucus by the serous and mucous cells.

We know from the study of histological sections that such chronic bacterial infections of mucous membrane as tuberculosis are characterized by finding the offending organism in considerable numbers in the mucous glands. It seems reasonable to assume that this is due, in part at least, to the greatly reduced flow of mucus from the dysfunctioning glands. By the same token, is it not safe to conclude that those pathological organisms invariably present as secondary invaders in this type of disorder will also tend to lodge and multiply in the mucous glands? If so, this would explain the success of that form of treatment designed to stimulate the secretion of these glands. It is my opinion that the excess mucus commonly found in the nose in hypertrophic rhinitis is due to the failure of the cilia to remove that which has been secreted, rather than because of hypersecretion. At this point in the pathological process, the condition is still reversible. If allowed to continue there results an infiltration of connective tissue, not only about the veins and lymphatics, but generally throughout the tunica. As this stage appears the condition is going over from true hypertrophy to hyperplasia. The pathology of hyperplastic rhinitis will be discussed under that heading.

The leading symptom in hypertrophic rhinitis is nasal stuffiness. The obstruction may be complete or partial, unilateral or bilateral. The tendency to shift from side to side as seen in simple catarrhal rhinitis is not so common. It is almost always much worse on lying down. Because of the thick postnasal discharge, these patients often complain of a cough which is nonproductive and also aggra-

vated upon assuming the recumbent position. Laryngeal changes occur which give rise to varying amounts of hoarseness and clearing of the throat, both of which are more often due to the collection of tenacious mucus about the vocal cords rather than to a true laryngitis. The presence of infected post nasal mucus frequently gives rise to a sore throat, typically worse on awakening in the morning and becoming more comfortable after breakfast when the mucus has been temporarily removed. Headache is also a common symptom. Most often it is frontal, over the bridge of the nose, over the antra or behind the eyes; or a combination of any of these. In order to make breathing more comfortable, patients usually resort to hard nose blowing. This may only serve to increase the intensity of the headache or produce involvement of the eustachian tubes. Acute exacerbations, as seen in the intumescent type, are not the rule here, but attacks of sneezing do occur which are followed by a temporary increase in the nasal congestion. Excoriation and fissuring of the nares is often a source of discomfort as well as repeated attacks of furunculosis about the vibrissae. As is the case in similar situations where a focus of infection exists, the leading complaints are commonly lassitude, easy fatigability and anorexia. Anosmia may be present but is not common.

On inspection the nose has a characteristic appearance. Because of the venous congestion, the membranes have a deep red color. The presence of more than the normal amount of mucus gives the entire mucosa a glistening appearance with strands of mucus seen extending from the septum to the turbinates. On the floor of each nostril many times one finds a pool of stagnant, glairy mucus. True pitting edema can be demonstrated by pressure placed on the inferior turbinate. The middle turbinate is usually less involved. Unlike the intumescent type, there is no marked and rapid reaction to the application of various decongestants. Because of the presence of secondary invaders, there is sometimes an odor, in my experience this is not very common. As might be expected there is a high incidence of deviated septum, adenoids and other causes of chronic nasal obstruction as mentioned earlier.

It goes without saying that prevention is more important than any attempt to cure. Therefore, it is up to us as rhinologists to check when possible every case of simple catarrhal rhinitis, to put an end to repeated acute infections of the nose, and to try to keep the general resistance of our patients at a good level. However, when confronted with a hypertrophic rhinitis case we should direct our conservative treatment toward two broad goals; the first to restore normal nasal physiology, the second to improve the general condition of

the patient. To accomplish the former, office treatment is of inestimable value.

It has been my practice to first decongest the membranes with a cotton pack soaked with a solution of cocaine 5% and neosynephrin ¼% in equal parts. After this has been left in place about ten minutes the nose is well opened and quite well anesthetized This is followed then by a pack containing a solution of argyrol 20%, ichthyol 2% and glycerine 20%.

After this has remained in place about fifteen minutes the patient will then usually be able to blow out a large amount of thick, glairy mucus. Theoretically at least, the mucous glands have been stimulated to secrete and empty themselves of inspissated mucus and saprophytic bacteria. The nose is then flushed out with a spray of normal saline and further cleansed with tip suction. Rather than use a spray of penicillin I prefer to use a solution in the strength of 2000 units per cc introduced by the Proetz displacement technique. My preference is based on the fact that with this technique, the penicillin circulates through the meatuses where it can reach any sensitive bacteria and also wash away any tenacious mucus present. The fact that a certain amount enters the ethmoid labyrinth during this procedure is of doubtful value, but can certainly do no harm. This treatment should be repeated two times a week.

Local treatment to be carried out at home consists in penicillin nose drops of the same dilution, a suitable eye wash, and shrinking drops such as neosynephrin ¼%. The penicillin drops I prescribe at the rate of five drops four to five times a day to be continued for ten days. As before mentioned, it is my personal feeling that the lacrimal duct, tear sack, and the conjunctiva act as a definite focus for secondary infection in this type of rhinitis, and must be treated if one expects any results in the nose. The decongesting nose drop is advised for night use only. Continuous use of such drops will definitely aggravate this condition for reasons before mentioned.

A suitable gargle is also frequently helpful to clear away the mucus which collects on the pharynx. What other measures can be employed to help rid the nose of its secondary infection? Occasionally an autogenous or stock vaccine is helpful. High doses of vitamin A as described before, hyposensitisation to any offending inhalants, especially dust in this case, and the elimination of any sensitizing foods is important. Complete abstinence from alcohol is most important; it has been my observation that even as little as one drink will upset the progress of recovery, yet when recovery is complete, the ingestion of alcohol has no tendency to induce a recur-

rence. Complete abstinence from all forms of smoking is to be desired, but in my experience one is forced to settle for something less than that in most cases. During the winter the patient is urged to keep his bedroom at even temperature.

As described under simple catarrhal rhinitis, an exhaustive search for any general physical illness should be made, and if found, corrected. It again should be emphasized that the proper attention to any mental or emotional factors should not be overlooked. The importance of additional rest must be brought home to the patient.

In the event that anatomical abnormalities are present in the nose, the correction of these is best postponed until the rhinitis is much improved or has been cleared completely. Nevertheless, it is not always possible to do this, for not infrequently a cure cannot be brought about until such measures have been taken. A hypertrophic rhinitis in itself need not be considered a contraindication to necessary surgical procedures such as submucous resection of the septum, submucous resection of the enlarged turbinal bone, removal of hypertrophied tips, cautery of the inferior borders of the inferior turbinates, etc. In a certain number of cases no assortment of therapy will avail and the hypertrophic state will either persist or go on to a hyperplastic rhinitis.

HYPERPLASTIC RHINITIS

A hyperplastic rhinitis may either be the result of an unresolved hypertrophic rhinitis, or the result of an unmanageable allergic vasomotor rhinitis.

If the perivenal and perilymphatic cuffing continues, certain irreversible changes occur. The perivascular infiltration gradually leads to the ingrowth of connective tissue about the vessels and actual thickening of their walls. In the meantime the arterial supply has not been reduced so the accumulation of transudate continues. Under the weight of this prolonged increased fluid content, the mucous membrane prolapses in certain areas. In this way polyps or polypoid degeneration of the mucous membrane comes about.

With the resultant further interference with circulation and nutrition and increasingly present secondary infection, these areas may organize and become firm masses of edema fluid and connective tissue. Sooner or later the continual distension of the tissues with fluid creates pressure on the arteries themselves and the normal supply of blood is reduced. This causes the familiar pale, rather cyanotic color seen in this type of rhinitis. As the process continues further, the entire mucous membrane all the way through to the tunica be-

comes infiltrated with connective tissue. This describes the pathology in those cases that have resulted in long standing hypertrophic changes. The process involved when it is due to vasomotor phenomena is at the present little known or understood.

The symptoms arising from this disease are essentially the same as those described for hypertrophic rhinitis. Perhaps a noteworthy exception is that variation in the nasal congestion from one side to the other or in degree is rare, since the changes in the turbinates are more or less fixed.

There are definite signs, however. In the first instance involvement of the nares is common and usually marked. It consists of painful fissuring and excoriation. The membranes themselves have a typical pale cyanotic color. Often there is no pitting edema since the mucous membrane has become polypoid and organized. Such changes are most often seen along the inferior border of the middle and inferior turbinates. The posterior tip of the inferior turbinate is also a familiar site for polypoid degeneration. The presence of actual polyps is common. These may arise either from the nasal mucosa or from the mucosa of a coincidentally diseased sinus.

Because of long standing points of pressure, areas of the membrane become ulcerated, or microscopic examination will show metaplasia of the ciliated pseudocolumnar epithelium to stratified squamous. Such points usually occur where the middle or inferior turbinate has been in long contact with the septum. In this condition ciliary activity is even further impaired. As might be expected, the presence of anatomical abnormalities causing chronic obstruction is the rule since their presence in many instances was directly responsible for the hyperplastic state. Microscopic study of the tissue or mucus will frequently show the presence of eosinophiles. Some workers believe this indicates an allergic mechanism as the cause, others disagree and feel that this type of cell may be present as a result of chronic inflammation. Personally I feel that an eosinophilia indicates allergy.

Treatment of a hyperplastic rhinitis should not be directed towards restoring normal nasal physiology for this is not possible. The condition has gone too far for that and the underlying pathology is irreversible. Therapy should aim at giving the unfortunate patient as much nasal comfort as possible. Various surgical procedures are the best attack. These include the removal of polyps, trimming of the inferior borders of the turbinates, removal of enlarged posterior tips, crushing or fracturing turbinates, cautery or electrodessication of obstructing turbinates, etc. Because of the coincidental hyper-

plastic sinusitis that often exists, various radical or conservative surgical approaches are many times indicated. Such existing sinusitis must be irradicated to obtain the best therapeutic results. After such steps as are indicated have been done and the patient has a permanently patent airway on both sides, the pooling of stagnant mucus may be prevented by periodic tip suction or gentle saline irrigation in the office. Some patients can be instructed to irrigate their nose at home without causing harm.

ATROPHIC RHINITIS

One of the most difficult problems facing the rhinologist is atrophic rhinitis. The etiology of this condition is not definitely known. Recent research suggests that it is the result of an inflammatory process which begins in childhood. To quote from Eggston and Wolff, "The causes of the inflammation are primarily the exanthematous diseases of childhood and infection by pneumonia and influenza bacilli, all of which have a pronounced rhinotropic tendency in man." The nasal disease accompanying an exanthematous infection is usually a hypertrophic type which may remain latent throughout life, or may go on at some later time to an atrophic rhinitis.

That atrophic rhinitis is but a progression in the pathology already found in the hypertrophic type seems reasonable. In the former condition histologic study shows further perivenal and perilymphatic sclerosis, to the point of complete obliteration. Beyond that there is seen the characteristic changes in the terminal arterioles. This consists in perivascular changes similar to that affecting the veins and lymphatics. Circulation through these vessels is further impeded by an active endarteritis obliterans. This is in the form of an obstructing connective tissue proliferation which occurs not only in the media of the vessel wall, but in the intima as well. Being terminal vessels, collateral circulation is practically nil, and a marked alteration in the nutrition of the mucosa ensues. This results in a metaplasia of the surface epithelium from ciliated pseudostratified to unciliated squamous. There is a reduction in the number of mucous glands and goblet cells and a marked thinning of the tunica, both because of the contraction of the scar tissue that moves in and because of the marked reduction in interstitial fluid. The end result is obviously an irreversible loss of nasal function. Ciliary activity is gone, the inferior turbinates have lost their ability to act as nasal valves, the supply of mucus is far below that required to properly humidify the inspired air. Secondary infection soon follows. The bacteria found are doubtless the result rather than the cause of this distressing disease.

Even though the nasal chambers are widely patent at all times, one of the leading symptoms of this condition is nasal stuffiness. The sensation of clear breathing results from the drop in temperature created by the flow of inspired air as it evaporates the nasal mucus. This sensation is, of course, completely absent in the case of atrophic rhinitis. The bad odor is the result of marked secondary infection which is fostered not only by the total loss of nasal function, but also by the formation of crusts under which the saprophytic invaders may remain unmolested. Typically, patients afflicted with this disease, make repeated efforts to clear the nose of crusts by blowing the nose. Because the wiping action of the soft palate has been destroyed by the absence of mucus, constant and useless hawking results. In the absence of proper conditioning of the inspired air by the nose, secondary pharyngitis, laryngitis, and tracheitis are commonly seen. Pains and aches in various parts of the head are common. These are due to neuralgias created by eddies of air set up in the nose upon inspiration. With the total air capacity of the nose greatly and permanently increased, the normal flow of inspired air cannot occur. Anosmia is common.

When can one say that a nose is atrophic or that it is not? It is my opinion that when the examiner, upon looking into the nose, is able to see the nasopharynx the membranes are atrophic. There are factors that must be kept in mind in this regard. One must be sure that the patient has not used decongestant nose drops a few hours prior to the examination. Furthermore, an initial visit to the physician is often accompanied by a certain amount of apprehension, this too will act to decongest the nose in certain instances. In addition, the initial or decongested stage of an acute coryza must be kept in mind. All degrees of atrophy may be seen. In the earlier cases the capacity of the nose is increased, but the mucous membrane still retains its more normal velvety appearance. In the terminal stages there is marked atrophy of all the turbinates, the membranes have a slick, shiny appearance, and the interior of the nose is coated with thick green putrid crusts. The ozena seems to vary directly with the amount of crusting present. Secondary changes in the nasopharynx, pharynx, and larynx are the rule and appear injected, dry, and crusted as a result of the constant exposure to the unhumidified and cold inspired air.

Once the condition has become a true atrophic rhinitis, there is no hope of reversing the process. Treatment is directed entirely to keeping the nose clean and as free from crusts as possible; also to keeping to a minimum the secondary changes that occur in the rest of the respiratory tract. In other words, institute measures which

will tend to act as substitutes for the functions of the normal nose. The nose can best be kept clean by saline nasal douches. These can be done by the patient at home. In the office a more thorough job can be done by following the douche with tip suction under direct vision. Moisture is satisfactorily added by using drops advised by Proetz. These are alcohol 5%, glycerine 3%, sodium chloride .9% with a few drops of scent added. In my experience, the use of a dropperful several times a day, is far superior to any oil, estrogenic or otherwise. This mixture not only tends to replace sorely needed moisture, but helps a great deal to keep down the crust formation. In the winter time, because of the increased lack of moisture in the air, it is often helpful to supplement these drops with steam inhalations. This combination will go a long way in keeping to a minimum the troublesome secondary changes in the larynx and trachea. Attempts to reduce the size of the nasal chambers by surgical measures has not proven to be of value with one possible exception. If the condition is largely unilateral and on the side of a marked concave deviation of the septum, it is helpful to correct the septal deformity. The atrophic side can further be reduced in size by replacing the septal cartilage with its convex surface toward it. Infection of the sinuses frequently complicates this disease. When present it should be eliminated as far as possible.

It has been the purpose of this paper to bring emphasis to the field of rhinology, to correlate diseases of the nose with normal nasal physiology, and to present the facts and a few of my own theories on the subject in such a way as to clarify the approach to diagnosis and treatment.

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VIII

THE VESTIBULAR RESPONSES TO TURNING, WITH NOMOGRAMS FOR THE DETECTION OF STREPTOMYCIN AND OTHER DRUG TOXICITIES AND FOR THE PREDICTION OF THE NORMAL VARIATIONS OF NYSTAGMUS AND VERTIGO

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Testing of vestibular function has become a valuable adjunct to neurologic and otologic diagnosis. Recently it has assumed importance in the detection of early toxic manifestations of certain drugs, notably streptomycin and dihydrostreptomycin. The rotational tests are widely employed in such evaluations of vestibular function. However, results of testing are often difficult to assess critically since little is known of the variation to be anticipated in normal persons subjected to vestibular examinations on several different occasions. For example, if a patient with a neurologic lesion, or receiving streptomycin, shows a decrease in rotational test responses from one week to the next, the question arises whether the decrease is due to the course of the disease, or the action of the drug, or whether it lies within the normal range of variability for that individual. No answer to this problem can be found in the literature. Only general statements[1] as to the normal limits of the duration of postrotational nystagmus and vertigo (usually given as 15 to 35 seconds) are available.

The effects of repeated rotation on the duration of postrotational nystagmus and vertigo have been extensively studied previously. Barany's[2] original papers describe parameters of response

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to repeated turning for a group of 60 clinic patients. However, an unspecified number of them suffered from "central vertigo." In addition, no details as to the frequency of examinations, or the time intervals between them, are given. Griffith[3] in 1920, turned 10 subjects rapidly 10 series of 10 turns each, every day for a number of days. He found that the duration of nystagmus and vertigo decreased from day to day. The major portion of the decrease occurred within the first few days. There was also a falling off in response within the period of 10 trials in any single day. In 1923 Dodge[4] made similar observations. Unfortunately there seem to be no reports in the literature on the results obtained when normal persons are turned in an accepted clinical manner at what might be clinically useful intervals.

We have subjected 104 normal adults to the Barany turning test 225 times in an attempt to answer the question of the degree of variation of response within the same individual. As a result of this study, we are able to present here nomograms giving the normal limits of variation for an individual with any given initial duration of nystagmus and vertigo. These nomograms have proved valuable in indicating the early occurrence of streptomycin toxicity even before the onset of the vestibular symptoms.

METHOD

One hundred and four white, normal senior medical students, graduate nurses, and medical faculty members of the University of Pennsylvania served as subjects. Their ages ranged from 20 to 45 years. None of the females were pregnant, but all were in active reproductive life. They were examined when not menstruating. All subjects were examined one hour after lunch, and after as little ambulation in the previous 15 minutes as possible. The testing was performed in a quiet, evenly illuminated room of 68-72° F. (20-22° C.). Each subject was seated in a standard Barany chair, his head supported by a head rest, and flexed toward his chest so that the vertical axis of his head was 30 degrees forward and the external canthus of each eye was on a horizontal line with the ipsilateral tragus. With eyes closed the subject was then noiselessly turned at constant velocity, one turn per 2 seconds, for a total of 10 turns, in 20 $\pm$ 0.25 seconds. Following the rotation, the subject looked without visual fixation straight forward into the distance, and indicated the instant at which all sensation of rotation ceased. This was called the duration of postrotational vertigo. The subject's nystagmus was observed concomitantly, and its precise duration as noted by the unaided eye of the investigator was recorded. (The

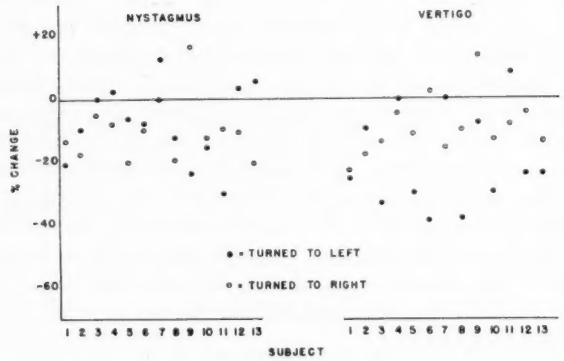

Fig. 1.—The effect on the duration of postrotational nystagmus and vertigo of repetition of the turning test two minutes after its initial performance. Only the results of the second test (both right and left turns) for 13 subjects are plotted. They are shown as the percentage change from the first test. Note that after the second examination there is usually a decrease (statistically significant)in the duration of both nystagmus and vertigo.

same observer was employed throughout the study.) Three minutes after the cessation of nystagmus and vertigo, the person was turned in a similar manner in the opposite direction. A single examination thus consisted of two rotations as just described.

RESULTS

I. *Normal Values* (Table 1).

A. Males. The mean duration of postrotational nystagmus was 22.9 seconds. The range was 11 to 42 seconds. The mean duration of vertigo was 20.9 seconds (range 7 to 38). There was no statistical difference in the results of turning to the right versus to the left for either nystagmus or vertigo. (Subjects were turned to their right first, i.e. clockwise, unless otherwise specified.) There was also no significant difference between right and left in 13 males who were turned initially to the left rather than to the right.

B. Females. The mean duration for the post-rotational nystagmus was 24.3 seconds (range 11 to 38). For vertigo the mean was 20.7 seconds (range 10 to 38). There was no significant difference between the values for males and females. For both males and females there was no significant difference between the durations of an individual's postrotational nystagmus and vertigo.

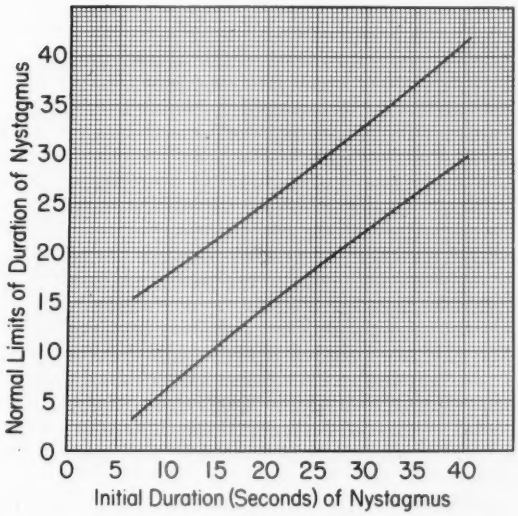

Fig. 2.—Nomogram for predicting the normal limits of variation in duration of postrotational nystagmus given the initial duration of postrotational nystagmus. 1. Locate along the baseline the duration of postrotational nystagmus for the first examination (use average of right and left turn). 2. From this point erect a perpendicular intercepting the two curves. The points of interception represent the normal limits of subsequent examinations for the individual being tested. 3. Read off along the left hand side of the graph the actual values in seconds.

II. *Repetition after two minute interval* (Fig. 1).

In 13 subjects, 2 minutes after the cessation of nystagmus and vertigo resulting from the turning test, the entire procedure was repeated. These paired data showed a small, but significant decrease in the duration of nystagmus and vertigo for the second examination ($P<.02$). The mean decrease for nystagmus was 2 seconds, for vertigo 2.5 seconds. The fourth turn, that is, the second half of the second examination, was not significantly different from the third turn (the first half of the second examination).

III. *Repetition after 30 minute interval.*

Thirteen males had the turning test repeated 30 minutes after its initial performance. After the first half of the second test the mean decrease for nystagmus was 0.3 seconds, for vertigo 1.4 seconds. These differences were not significant ($P>.05$). The mean decrease after the final turn of the second test was 1.9 seconds for

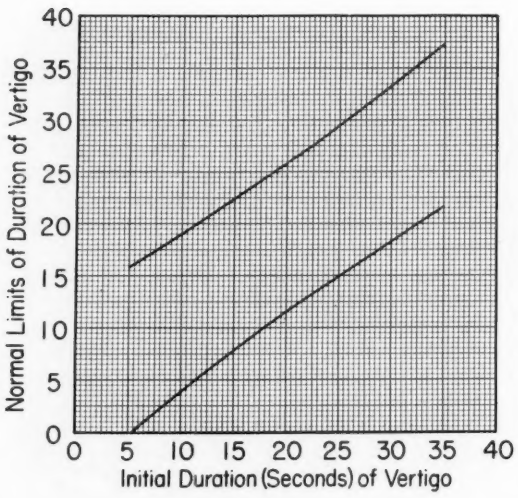

Fig. 3.—Nomograms for predicting the normal limits of variation in duration of postrotational vertigo given the initial duration of postrotational vertigo. 1. Locate along the baseline the duration of postrotational vertigo for the first examination (use average of right and left turn). 2. From this point erect a perpendicular intercepting the two curves. The points of interception represent the normal limits of subsequent examinations for the individual being tested. 3. Read off along the left hand side of the graph the actual values in seconds.

nystagmus, 2.0 seconds for vertigo. These changes were significant (nystagmus, $P<.02$; vertigo, $P<.05$).

IV. *Repetition after 1 week.*

The turning test was repeated on 32 males one week after the initial examination. There was no significant difference between the two examinations in the duration of either vertigo or nystagmus.

By the use of several statistical methods,* it was possible from these data to construct the nomograms in Fig. 2 and 3. Given the

*The direction of the turning did not influence the duration of postrotational nystagmus and vertigo (see body of this paper). Therefore, the results of the right and left turns for each individual were averaged. For the subjects studied, the correlation between the postrotational durations, obtained at an interval of one week was: nystagmus, 0.87; vertigo, 0.79. A regression equation (Ezekiel[6]) was next calculated for the prediction of subsequent values from initial values. The error of estimate of a single prediction was then determined. This permitted the setting of upper and lower limits of variation to be expected from any predicted value. These limits as given here will be correct 95% of the time for a given white, adult population similar to the one we sampled.

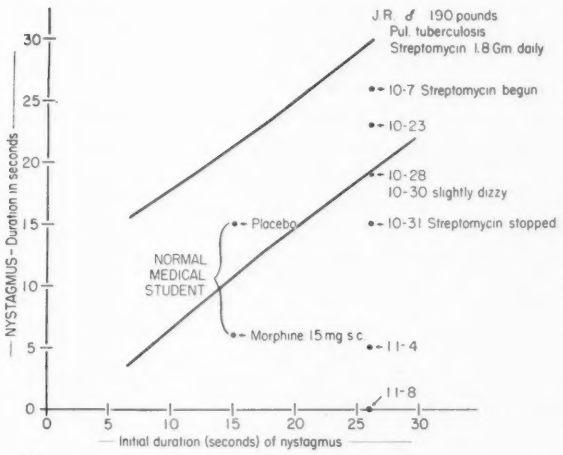

Fig. 4.—The nomogram applied to two cases. Note that J.R.'s duration of postrotational nystagmus falls below the lower limit on the nomogram before it falls below the conventional 15 second lower limit, and before the onset of vestibular symptoms. When plotted on the nomogram, the vestibular response of a normal medical student after a 15 mg. injection of morphine is clearly recognized as abnormal.

initial durations of postrotational nystagmus and vertigo for a normal individual, one can obtain from the nomograms the upper and lower limits to which the durations of nystagmus and vertigo may change on a subsequent examination and still remain within normal. These nomograms have been so constructed that the limits imposed by them will be correct 95% of the time for a given adult, white population similar to the one we sampled. In actual use, one locates along the baseline of the appropriate nomogram the initial duration (averaging the results of the right and left turns) of either postrotational nystagmus or vertigo obtained by turning the subject as described under METHOD. A perpendicular is erected from this point. The points at which the perpendicular intercepts the 2 curves on the nomogram represent the normal limits. The actual values in seconds are read off along the left-hand side of the nomogram.

Fig. IV shows the alterations in vestibular function of a patient (J. R.), who was receiving streptomycin for pulmonary tuberculosis. Note that the duration of postrotational nystagmus falls within the abnormal range on the nomogram before the onset of vestibular symptoms. Note also that at the point when the test results fall within the abnormal range on the nomogram, they are still within the normal

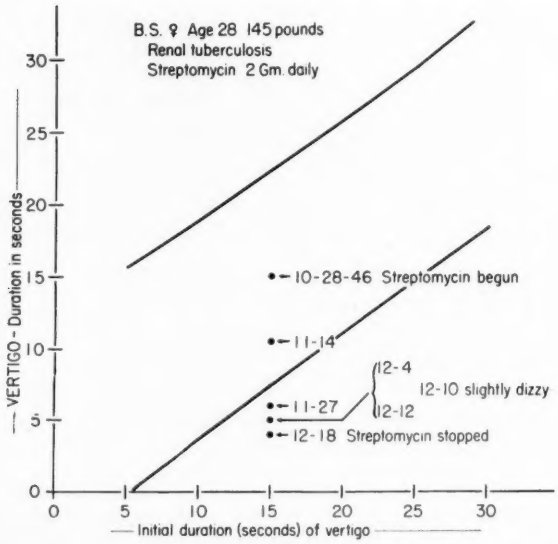

Fig. 5.—The nomogram applied to a case of streptomycin toxicity. Note that the vestibular responses when plotted on the nomogram fall below the lower limit two weeks before the onset of the patient's vstibular symptoms.

range (15 to 35 seconds) stated in texts of neurophysiology. Therapy was continued in this case until the onset of vestibular symptoms because of the belief that the Barany test results represented chance variations falling well within the normal limits defined by neurophysiologists. Fig. 5 shows the progressive decrease in the duration of post-rotational vertigo in a female receiving streptomycin for renal tuberculosis. Here the graph indicates an abnormal response 2 weeks before the patient's vestibular symptoms appeared. The duration of nystagmus in this case remained constant at 15 to 16 seconds. In the first case cited (J. R.), the duration of vertigo remained unchanged until the nystagmus had fallen almost to zero. The lack of a coincident change in nystagmus and vertigo in these subjects suggests that the vestibular disturbance produced by the streptomycin was at least partially central in origin (Winston)[7].

The abnormal vestibular response produced in a normal medical student by the subcutaneous injection of 15 mg. (gr. ¼) of morphine is clearly recognized when charted on the nomogram. Morphine more often decreased vestibular response to rotation to values which fell

within the lower normal limits of the nomogram (Rubin and Winston).[5]

COMMENT

These data indicate that the results may not be reliable if the turning test is repeated several minutes after its initial performance. Even a 30 minute interval may not suffice for critical work, since there was a statistically significant decrease in response for the final turn on re-examination after 30 minutes. However, results of tests performed one week apart were not significantly different.

Knowing the normal limits of variation in response (given in the nomograms), one can ascertain when a change in response is abnormal. This might prove useful not only in following the progression of neurologic conditions, or the effects of streptomycin therapy, but also in the evaluation of the effects of other drugs on vestibular responses.

SUMMARY AND CONCLUSIONS

1. Normal Barany turning test values for the durations of postrotational nystagmus and vertigo for adult males and females were presented.

2. The values for males and females were not significantly different.

3. The direction of the initial turning did not influence the test results.

4. There was a significant decrease in vestibular response when the test was repeated after 2 minutes.

5. There was a significant decrease in vestibular response to the final turn when the tests were repeated after 30 minutes.

6. The variations in responses to examinations performed one week apart were slight, and purely random in direction.

7. Nomograms predicting the normal limits of variation of turning test responses for a given initial test result were presented.

8. The application of the nomograms to vestibular testing during streptomycin therapy was shown.

9. The usefulness of the nomograms in recognizing streptomycin toxicity before the onset of vestibular symptoms was demonstrated.

10. It was suggested that the effects of other drugs upon vestibular function might be similarly evaluated.

We wish to acknowledge the aid and encouragement of Professors Carl F. Schmidt, Robert D. Dripps, and Harry P. Schenck.

Dean John McK. Mitchell and Dr. M. Valentine Miller kindly helped arrange for the medical students to serve as subjects.

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TABLE 1.—DURATIONS (IN SECONDS) OF POST-ROTATIONAL NYSTAGMUS AND VERTIGO. RIGHT AND LEFT REFER TO THE SUBJECT'S RIGHT OR LEFT AND INDICATE THE DIRECTION OF THE TURN.

SUBJECTS	NYSTAGMUS		VERTIGO	
	Right	Left	Right	Left
86 males				
mean	23.0	22.7	21.2	20.6
s.d.	5.7	6.1	6.2	7.1
18 females				
mean	24.2	24.3	20.7	20.6
s.d.	6.1	6.6	5.6	5.6

IX

THE ARTIFICIAL EAR DRUM

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There are literally thousands of cases of conduction deafness due to chronic otitis media in every large community. Most of these chronic infections resulted from complications following acute exanthemata, which means that the majority of these individuals have been deaf since early childhood.

Although the treatment of chronic otitis media has been extensively reported, it is significant to note that few suggestions have been offered for the treatment of the accompanying deafness. Patients with dry middle ears were congratulated on their good fortune and referred to the hearing aid companies for their complaint of deafness. Patients with good hearing and a chronic otitis media that did not respond to local therapy were reluctant to undergo a radical operation except in case of an emergency, for fear their hearing would be further jeopardized by the removal of their diseased but still functioning middle ear. Those that were dissatisfied with the electric hearing aid considered their cases hopeless, as they had already run the gamut of treatments with no appreciable improvement in their hearing.

However, extensive audiometric studies showed that the majority of these patients had excellent bone acuity despite the chronicity of their infection. Actually the deafness was due to an absent or diseased middle ear which mechanically prevented sound from reaching the cochlea. This led to the idea of replacing the destroyed or non-functioning sound conduction apparatus with a diaphragm rod prosthesis known as the artificial middle ear.[1] Unfortunately the artificial middle ear did not prove to be very practical in that the average ear canal was too narrow and tortuous to accept the insert. In view of the present limitations of the artificial middle ear, a less efficient but a more universal type of middle ear prosthesis was developed in the form of the artificial ear drum.[2]

The artificial ear drum is a soft, conical tube made from a rubber-like plastic known as Korogel. It is introduced into the ear canal until it makes contact with the yielding area of the exposed

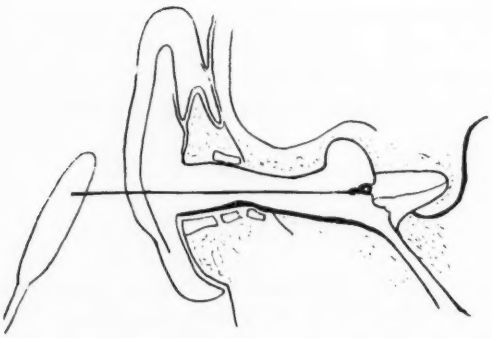

Fig. 1.—Drawing showing the acoustic probe in contact with the stapes in a case of chronic otitis media.

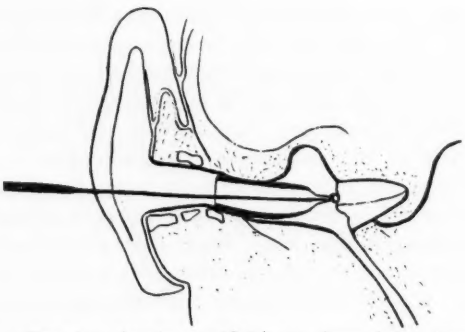

Fig. 2.—Drawing showing artificial ear drum being introduced into ear canal.

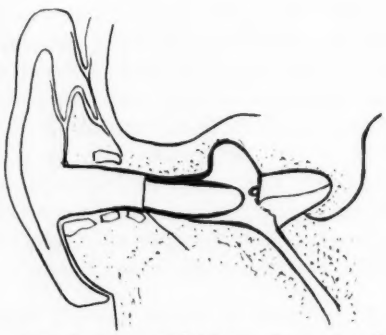

Fig. 3.—Drawing showing artificial ear drum that has lost contact with the stapes when applicator was withdrawn from ear canal.

middle ear which has been already established by the use of the acoustic probe,[3] (Fig. 1) and functions as a transformer, thus replacing the destroyed sound conduction apparatus.

The artificial ear drum is of no value to the patient regardless of his improvement in hearing unless he is able to introduce, remove, and care for the insert himself. No patient should be permitted to wear a plastic drum unless he can satisfactorily demonstrate to the otologist that he requires no assistance and is familiar with the proper technic of the plastic drum. Much time will be gained and the fitting will be less of an ordeal if the physician assumes that the patient knows nothing and carefully explains each step of the procedure (Figs. 2 and 5).

Using a proper sized artificial ear drum, which has been previously determined by the examiner, the patient is told that the plastic drum must be introduced into the ear canal until contact is made with the sensitive area. He should think of his ear canal as a clock and that his contact area on the right side is equivalent to ten o'clock while that on the left side is equivalent to two o'clock. If the ear canal is very narrow and tortuous, it may be necessary for the patient to widen and straighten out his own ear canal by pulling the ear with his opposite hand from behind his head.

A constant sound source such as a radio, loud clock, or running water is used as a guide to determine when he has made proper contact with the insert.

The patient then introduces into his ear canal by means of a cotton tipped metal applicator a proper sized artificial ear drum which has been lubricated with a thin coat of mineral oil. As soon as proper contact is made, he gently removes the metal applicator leaving the plastic ear drum in place. Sometimes the drum is partially withdrawn when the applicator is removed so that it has no contact with the sensitive area. This happens when there is too much cotton on the tip of the applicator or if the applicator is withdrawn too quickly. Practice and patience may be required before the patient is able to perform the procedure without difficulty.

The plastic drum is removed with a pair of small forceps, washed in lukewarm, soapy water, and dried with tissue paper.

In ideal cases the insert is as efficient as an electric hearing aid with the added advantages of being invisible and requiring neither wires nor batteries. It may now be purchased commercially and is available in many different, standardized sizes and shapes so that practically any ear canal can be fitted with an artificial drum.

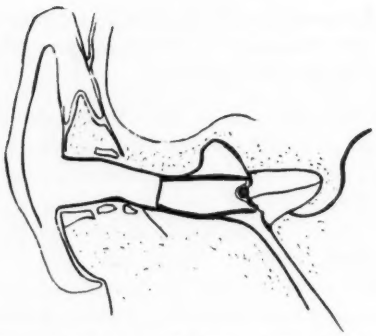

Fig. 4.—Drawing showing artificial ear drum that has been inserted improperly into the middle ear.

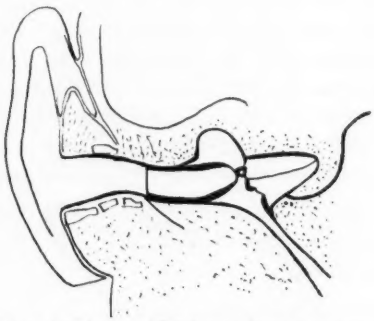

Fig. 5.—Drawing showing artificial ear drum in proper contact with stapes.

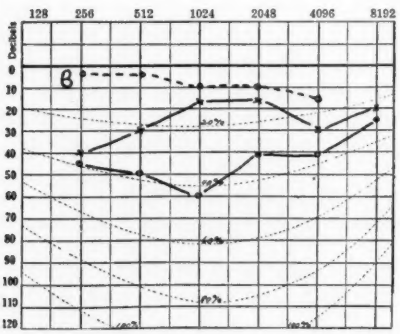

Fig. 6.—Audiogram showing the effect of the artificial ear drum on case of chronic otitis media.

A chronic discharging ear is not a contraindication to the use of the artificial ear drum. However, it is extremely important to impress upon the patient that the plastic drum must be removed each night before retiring. This is a hygienic necessity as the insert may bring about an exacerbation of the chronic infection. The patient should be appraised of the danger signals of extension such as headache, pain, vertigo, or an increase in discharge. If any of these symptoms develop, he should remove the prosthesis and consult his otologist.

We should not lose sight of the fact that the artificial ear drum is only performing as an inefficient substitute for the destroyed, diseased middle ear apparatus. Practically every patient with chronic otitis media who obtains an improvement in hearing with the plastic drum would be further benefitted if he were able to accept a diaphragm rod prosthesis. There are also numerous patients aided by the acoustic probe, who cannot accept even the plastic drum, as the sensitive area is partially concealed by an overhanging remnant of ear drum which prevents proper contact with the insert.

This means that a surgical procedure should now be devised to deliberately leave a post-operative mastoid and middle ear cavity that will easily accept some type of diaphragm rod prosthesis.

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X

A CONCEPT OF ALLERGY AS AUTONOMIC DYSFUNCTION SUGGESTED AS AN IMPROVED WORKING HYPOTHESIS

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It is important to remember that allergy has two aspects, the one clinical, the other immunologic. It is perhaps unfortunate that some allergists in turning from the one to the other aspect appear to insist that treatment of patients shall be carried exclusively along immunologic lines although the diagnosis may have been made entirely on the basis of a practical clinical empiricism. The allergist in his quality of immunologist has broadened our understanding of physiologic mechanisms that have to do with the organism's intolerance to interference from without. The immunologist in assuming the character of clinical allergist, however, often has seemed to be too rigidly insistent on the immunologic dogma that all the clinical manifestations that have become known as the allergies must have an antigen-antibody mechanism as a background of etiology and as a basis for treatment. Relatively recently the value of a clinical approach to many of the problems of allergy has received attention. Study of those factors that alter the threshold beyond which manifestation of allergy occurs, as Carryer[24] stated, has proved more fruitful in the care of many patients than has sole dependence on an antigen-antibody type of treatment. Nevertheless, most allergists insist on including an immunologic mechanism in the definition of allergy, although it seems probable that few of them insist on the demonstration of an antigen-antibody mechanism in making a clinical diagnosis of the condition.

I believe that this attempt to play the dual role of scientist and physician without separating the two parts sufficiently has caused some of the confusion in regard to the management of allergy. It seems to have been forgotten that the immunologic hypothesis was developed to explain certain syndromes whose confines had previously been laid out not by controlled experiment but on the basis of knowledge gained through observation and experience.

Read at the meeting of the American Academy of Ophthalmology and Otolaryngology, Chicago, Illinois, October 8 to 13, 1950.

Von Pirquet's[76] hypothesis of allergy was based on the discovery of hypersensitivity in an immunized organism. He, however, considered these two terms to be mutually exclusive. It seemed impossible to him to consider as immune an organism which is protected against a disease, and at the same time is considered reciprocally hypersensitive to the same disease. This phenomenon could not be termed a paradox, he stated, because the word "paradox" should be applied only to an exceptional case, whereas the more one entered into this field of inquiry the more the "according to lawness" of the phenomenon was recognized to be. He, therefore, suggested a new, general, nonprejudicial word for the change of condition which the organism accomplishes, perhaps through the agency of an organic, living or lifeless toxin. According to von Pirquet[77] all that could be stated with certainty about a hypersensitive organism is that its readiness for reaction is altered. For this general concept of altered reactivity he suggested the expression, "allergie." Von Pirquet showed himself willing to alter details of the hypothesis as new observations were presented. Some of his followers, however, have not exhibited his intellectual adaptability.

Carryer[24] stated that internists vitally interested in the problems of allergic disease are keenly aware of the shortcomings of a purely immunologic approach. He stated, however, that inasmuch as the investigative thought over the past four decades has been greatly influenced by those whose background and experience were in the field of immunology, it was not difficult to understand why progress has been directed away from the nonimmunologic aspect of allergic disease. He recommended a critical review of the none too gratifying results of current, generally accepted and practiced tenets which have shortcomings of considerable magnitude.

DEFINITIONS AND DESCRIPTIONS OF ALLERGY

In considering the desirability of substituting a new and more flexible hypothesis for the antigen-antibody reaction, a review of some representative definitions and descriptions of allergy made by proponents of the immunologic hypotheses may prove useful. Rostenberg,[87] for instance, recently stated, "The best definition for allergy is the following one: 'Allergy is an acquired specific alteration in the capacity to react which is predicated on an antigen-antibody mechanism.'" In his opinion, failure to include the antigen-antibody reaction has been the major reason for the confusion and lack of clarity which exist concerning the meaning of the word allergy. He wished it to be clearly understood, however, that in the majority of allergic reactions an antigen-antibody mechanism is not demonstrable by any known technics. This, he stated, does not

mean that antibodies do not exist in these states but merely means that we do not have as yet an appropriate indicator system to reveal their presence. He divided allergy arbitrarily into three immunologic patterns, the anaphylactic, the bacterial, and the eczematous type. He emphasized that it was important to realize that no clinical condition corresponds exactly to any one of the immunologic patterns listed. Many clinical conditions represent a combination of several of these types and, indeed, he considered that many varieties of allergic reactions do not fit into any of the three types given, but since there is so little information about them they cannot be set up as immunologic or allergic entities.

Rostenberg[87] does not give a single instance in which he considered that treatment of cutaneous allergic disorders by immunologic methods was certainly beneficial.

Rostenberg then appears to declare that although factual data in regard to the presence or absence of an antigen-antibody reaction are absent in many of the conditions he considers allergic, conclusions arrived at by extrapolation and inference can be depended on to be correct and that such conclusions will serve to clear up the confusion and lack of clarity which exists concerning allergy. According to Bell,[14] however, extrapolation and inference have been the chief causes of the major errors in human thought.

On the other hand, Harley[44] stated that in his opinion the confusion and lack of clarity in regard to allergy were owing to the tendency of allergists to invent new and perplexing terminology for phenomena which were fundamentally the same. In the present state of our knowledge it seemed to him impossible to give an exact definition to the term allergy.

The unitarian theory which was developed to do away with some of the confusion of terms appears to have gained wide acceptance. As Zinsser, Enders and Fothergill[120] stated, this concept of allergy implies that the injection of an antigen into the tissues of an animal will lead to the development of a single antibody capable of producing the various manifestations of antigen-antibody union. This formulation has been further modified so that the various antibodies are considered to represent varied physicochemical changes in the same globulin.

Kahn[50] embraced the unitarian theory of allergy, but to the previous concepts of cellular immunity suggested by Metschnikoff,[67] and the humoral immunity suggested by von Pirquet,[76] he added the concept of the third type of immunity or tissue immunity. He rejected the suggestion that specialized cells would be entrusted with

the entire defense of the body, stating that from the standpoint of phylogeny it would be reasonable to suppose that all cells possessed in some measure the ability to defend themselves against environmental stress whether that stress presented itself in the form of invading microorganism or some other form. He suggested that immune gamma globulin should be considered to be of two types, one of which is insoluble because it remained fixed in the cell, the other of which is soluble because it was dissolved in the blood serum and constituted the circulating antibody. Kahn also considered that the differences between bacterial allergy and allergy in which circulating antibody can be identified were in degree rather than in kind. Allergy in his opinion is merely an instance of hyperimmunity and there are many examples of overaction of a normal physiologic mechanism.

In Bronfenbrenner's[16] opinion, the accumulated evidence indicates that whenever antigen-antibody reactions occur in vivo there is always a concomitant injury to the tissues of the host, as evidenced by both local and general symptoms. It appeared likely to him that the very mechanism which causes this injury to the host is also instrumental in bringing about such protective effects as the warding off of infection by immobilization of antigen by the antibody. Basically this injury consists of an inflammatory reaction which is evoked by the physicochemical changes in the environment and differs from ordinary inflammation only by its rapid onset and relatively stormy course. This inflammatory process is accompanied by both local and systemic symptoms resembling those elicited by the administration of histamine. Because of this resemblance and especially because of the highly suggestive experimental demonstration of the presence of histamine-like substances at the site of antigen-antibody union, he believed that the most widely held view today is that the inflammatory reaction is actually due to the liberation of histamine-like substances from antibody-laden tissues when they come in contact with the specific antigen.

Bronfenbrenner also stated that phenomena called immunity and anaphylaxis are in fact merely different expressions of the same basic process of antigen-antibody union. Difference in the final outcome depends only on the extent and speed of this union and the consequent intensity of the injury to the host. Classical anaphylaxis as observed in animals and occasionally in man in his opinion is a laboratory artefact. Under natural conditions of exposure antigens enter tissues of allergic animals and of human beings much more slowly and in extremely small amounts; consequently their union with antibodies is less explosive and the injury to the host is much

milder than in classical anaphylaxis. The symptoms elicited vary in form depending on the portal of entry, and the amount of antigen on one hand and on the relative local sensitivity of the involved tissues on the other. When so exposed some individuals respond more easily to such immunogenic stimulus than others and these individual differences in reactivity seem to be determined by inheritance. The tendency to hyperreact is inherited, not the specific sensitivity itself.

A new hypothesis has been suggested by Wiener.[116] He stated that experimental work in relation to agglutinin and blocking antibody was the first definite demonstration of the incorrectness of the unitarian hypothesis of allergy. The evidence presented by his own work indicated that univalent and polyvalent antibodies are distinct entities as shown by the fact that they can be separated by natural means such as placental filtration. He pointed out that Witebsky[118] and associates partially separated these antibodies by dialysis in cellophane bags against distilled water. While the agglutinin proved to be associated principally with the resulting precipitate which contained most of the globulins, the blocking antibody or conglutinin remained mostly in the supernatant fluid together with the albumin.

Wiener[116] offered the following criteria for allergy based on his theory:

1. The normal (nonallergic and nonimmune) state is that in which the body contains no induced antibodies specific for the antigen in question. Cognizance is taken, however, of so-called natural or normal antibodies.

2. The immune state is one in which the body has acquired large amounts of antibodies of the blocking type formed in response to the introduction of antigen into the body by either natural or artificial means. In this state an excess number of univalent antibodies are free in the plasma and other body fluids.

3. In the allergic state the body contains sensitizing (bivalent) antibodies attached to cells, with little or no free univalent antibodies in the body fluids.

4. Hyposensitization is the process of converting the allergic state into the immune state by repeated injections of antigen at sufficiently wide intervals to stimulate the production of potent blocking antibodies. This treatment is succesful only when the subject achieves an adequate level of free univalent antibodies in his or her body fluids.

5. Desensitization consists of the injection of progressively increasing doses of specific antigen in rapid succession in order to sat-

urate antibodies attached to body cells. This method, besides being dangerous, is often unsuccessful and the refractory state that ensues is only temporary, due to the subsequent production by the body of additional bivalent antibody.

This hypothesis appears to combine Kahn's concept of tissue immunity with the concept of humoral immunity. Wiener pointed out a number of problems in immunology, previously unanswerable, that can be explained in the light of his new hpothesis.

While all these commentators differ considerably among themselves as to what constitutes allergy, they all insist that definition of the term allergy must contain a reference to an antigenic mechanism.

It is clear from a review of the literature of allergy, however, that the diagnosis of allergy in the clinic depends not on immunologic tests but on a well-taken history and careful observation of the patient.[4, 26, 35, 47, 68, 79, 104, 108] It is obvious that Rostenberg,[87] for instance, in classifying the various dermatologic allergies is depending on history and observation, else he would not so carefully point out that in the majority of such patients immunologic evidence is unobtainable.

In discussing skin tests in diagnosis of allergy Tuft,[104] while insisting that they are of value in diagnosis when they can be obtained, pointed out that as in other laboratory tests the results must be correlated with the history and other clinical findings before an accurate diagnosis is possible. He found that unless a positive reaction can be obtained repeatedly, such a reaction cannot be considered specific, but must be attributed to faulty technic, contaminated syringes, or irritating extracts. He divided all specific positive reactions into (1) nonclinical positive and (2) clinical positive. It seems clear that Tuft has made the diagnosis of allergy on the basis of clinical empiricism and merely hoped for confirmatory and possibly more specific information from skin tests.

Hansel[41] tacitly admitted that as a rule the diagnosis of allergy is made from clinical grounds alone when he stated that eosinophilia of the nasal secretions is the most dependable sign of allergy. The exact role of the eosinophil in allergy appears to be unknown. Petersen,[75] however, stated that he was able to produce showers of eosinophils by causing localized tissue anoxia. This finding suggests that eosinophilia can hardly be considered an indicator of an antigen-antibody reaction however valuable it may be as a diagnostic test for allergy.

Fox, Harned and Peluse[37] in discussing borderline allergy obviously were not considering allergy as occurring only among those patients who gave evidence of an antigen-antibody reaction.

Physical Allergy. Not all allergists have insisted on an antigen-antibody hypothesis of allergy, however. Duke[33] stated that in his opinion in only a minority of patients with asthma, hay fever, urticaria, eczema and other manifestations of allergy can the source of the illness be traced definitely to contact with some material substance to which the patient is sensitive. He found that in the majority of patients, even after a most painstaking effort had been made through the use of history, physical examination, skin tests and clinical tests, the primary source of the disorder could not be shown to be sensitivity to substances, such as pollen, dander, foods, drugs or vapors. He was astonished to find, on the other hand, that a rather large proportion of patients with allergic conditions are sensitive specifiically and solely to the action of a physical agent, such as light, heat, cold, or mechanical irritation, and indirectly to the action of emotional perturbation and fatigue. He termed such reactions "physical allergy."

There is a tendency among allergists, however, to deny that physical allergy as defined by Duke should be actually considered an allergy. For instance, Bronfenbrenner[17] stated that in his opinion it is unlikely that any real allergy (production of antibodies) to light exists. He remarked that although several authors have claimed to have succeeded in transferring light sensitivity passively, the lack of proper controls minimizes the significance of such findings.

In studying physical allergy Swineford[101] stated that in his opinion physical allergy usually is an associated allergic condition and not a primary reaction. It might be pointed out, however, that the evidence he presented indicates that the antigen-antibody reaction is secondary as much as it does that the physical reaction is secondary. Since this is the only paper I have found in the literature purporting to show that physical allergy in some manner is secondary to antigen-antibody allergy, and because there are several reports to the contrary, it would appear that Swineford's[101] findings need confirmation.

Peshkin[74] observed that ten per cent of normal children reacted to skin tests with a variety of allergens. He also found that some of these immunologically positive children were later precipitated into acute episodes of clinical allergy by other presumably unrelated conditions, such as acute infections. He suggested that clinical reaction patterns, depending presumably on some other factor

than the antigen-antibody mechanism, needed to be developed before clinical expression of allergy could take place. He termed such non-clinical sensitivity para-allergy.

Urbach and Gottlieb[106] suggested the term pathergy to cover both physical and antigen-antibody allergy. Physical allergy was to cover those cases in which an antigen-antibody mechanism could not be demonstrated.

It would appear that Peshkin and Urbach and Gottlieb were trying to escape from the horns of the dilemma posed by making diagnoses of allergy on a purely empirical basis, while at the same time insisting on the strictest adherence to the antigen-antibody concept of allergy in theory.

Selye,[95] however, reviewed the extensive literature that suggests that the organism could develop specific and nonspecific crossed resistance to various irritants without an antigen-antibody mechanism and White[114] recently defined immunity to include resistance to physical stimuli in which an antigen-antibody mechanism apparently plays no part.

INADEQUACY OF THESE HYPOTHESES

Since it appears that allergists in general make the diagnosis of an allergic condition through history and physical examination, since the physical and immunologic allergies cannot be distinguished from one another by these means, and since the majority of clinical allergies, according to Duke, fall into the group of physical allergies for which clinically significant skin tests are not obtained, does not insistence on the antigen-antibody concept of allergy tend to lead physicians into the error of unnecessarily doing repeated skin tests and treatments with various antigenic substances in cases in which such tests and such treatment could not be expected to be of clinical benefit?

Does not adherence to the antigen-antibody hypothesis tend to concentrate therapeutic attention on attempts at hyposensitization alone, or at least to methods by which the manufacture of sensitizing antibodies can be diminished while increasing the production of blocking antibody or to methods which tend in some manner to influence antibody formation? Empirically it has been observed that attention to general nutritional factors, the use of vasodilators, trace minerals and various vitamins as well as psychotherapy have appeared to influence allergic manifestations in individual cases. In cases in which these measures exert a beneficial influence and in cases which

are set apart as physical allergy is not the physician at a loss for a reasonable hypothesis on which to base treatment?

What can be the reason for this rather blind allegiance to the antigen-antibody hypothesis?

It seems to me that this attitude results from three factors. The first is respect to the memory of Clemens von Pirquet. The second is the impression that no adequate hypothesis for allergy is available to replace the antigen-antibody hypothesis. The third is based on the second and is the impression of many allergists that unless there are some stable reference points to restrain the diagnosis of allergy within reasonable bounds, the tendency to define allergy as a distaste for something or other, as in the lay expression an "allergy to work," cannot be successfully combatted. This seems an entirely reasonable attitude and, therefore, let us examine the second factor carefully. It would seem from the increasing acceptance of the unitarian hypothesis of allergy and the work of Cannon and Pacheco,[21] Cannon and Sullivan[22] and Walsh, Sullivan and Cannon[111] that von Pirquet's hypothesis has outlived its usefulness. Thus a different hypothesis whose fundamental assumptions are not in conflict with the knowledge gained in the forty years that have passed since von Pirquet presented his paper seems to be required. According to Bell,[14] this is the normal orderly progress of the scientific method of thought.

It might be well, therefore, to examine the available data to see whether a foundation can be found on which a new formulation can be erected that avoids the difficulties of the old. It would appear that the suggestion that allergy may be a form of autonomic dysfunction furnishes such a foundation.

RELATION OF AUTONOMIC DYSFUNCTION TO ALLERGY

The Autonomic System and Functions. Cannon[20] observed that the sympathico-adrenal reaction was one of the mechanisms by which the body tended to restore physiologic equilibrium or homeostasis when it was subjected to stress in either its external or internal environment. Petersen[75] further extended the concept of the autonomic system. He stated that while the mechanisms designed to meet the environmental stress are manifold, the vast majority of these reactions are primarily autonomic. Phylogenetically, he considered that the various means of autonomic integration must have taken origin in the following order:

1. The primary method, when the organism was unicellular or consisted of a few cells, was chemical and enzymatic.

2. As the organism became more complex and a circulatory system developed, substances we call hormones were produced which circulate in the fluids of the body. Their prime purpose is to speed autonomic reaction.

3. The third method evolved when autonomic correlative efforts required not only speed in the processes of integration or restoration of physiologic equilibrium, but direction of localization as well. For this purpose the anatomically defined autonomic nervous system, both sympathetic and parasympathetic, developed.

Petersen pointed out that these three components of the autonomic system are functionally inseparable; no disturbance can occur in any one element without immediately affecting the other two. He also noted that whatever autonomic alteration took place was immediately reflected in the behavior of the peripheral vascular bed, the arterioles, capillaries and venules. These reacted to environmental stress in a stereotyped manner, whether the stress arose in the external or the internal environment and whether it was due to physical agents, emotional perturbation, the invasion of micro-organisms or of nontoxic protein substances.

The existence of this stereotyped vascular reaction has received abundant confirmation.

By means of the method of Lombard,[61] observation of the functional reaction of the peripheral vascular bed to stress has enlightened us as to the fundamental functional changes resulting from the attempts of the organism to re-establish physiologic equilibrium or homeostasis. These were completely obscured as long as the pathologist restricted his observations to dead, fixed tissues.

Ricker and Regendanz,[83, 84] for instance, found that a typical stereotyped vascular reaction was present in inflammation of all types, and that an inflammatory reaction could not take place in tissue in which autonomic denervation had been done. They observed that in mild inflammation there was arteriolar and capillary dilatation with hyperemia. In somewhat more severe inflammation the arterioles were constricted with a slowing and clumping of the formed elements of the blood. In severe inflammation they found arteriolar spasm with dilatation of the contiguous capillary and venule. According to Oertel,[71] they gave convincing answers to criticisms of their findings.

Carrier[23] observed these same peripheral vascular reactions on exposure of the organism to differing degrees of cold.

Brown[18] observed this same type of arteriolar and capillary reaction in Raynaud's disease. He stated that this reaction represented a disruption of the normal co-ordination between arteriole and capillary. Krogh[57] has shown that the capillaries have an independent autonomic nerve supply and their caliber constantly changes. He also brought forward evidence indicating that the arteriomotor and capillomotor systems are able to respond in opposite directions to the same stimulus. Krogh noted that individuals exhibit a greater or lesser tendency to react to cold. He stated that although hyperreactivity may be a normal tendency in certain individuals this tendency can reach an abnormal level. Brown[18] also had found that in patients with the vasomotor neuroses the reactions to cold were similar to, but more marked than, the reactions of normal individuals and occurred at higher temperatures.

Mygind and Dederding[70] noted the same lack of coordination between arteriole and capillary in the skin of patients with Ménière's disease. They concluded that a similar reaction in the inner ear was the probable cause of the signs and symptoms of this disease. Lewis and Landis[59, 60] observed the same arteriolar constriction with capillary and venular dilatation in acrocyanosis. Fremont-Smith and his co-workers[38] observed complete stasis in all visible capillaries during a chill; this stasis was due to constriction of the terminal arterioles. Parrisius[72, 73] found lack of co-ordination among arteriole, capillary and venule in the skin of patients who had chronic simple glaucoma and Ménière's disease. Redisch and Pelzer[81] and Kennedy[53] found that while the premonitory symptoms of migraine might be due to vasospasm in larger vessels the characteristic headache seemed to be due to this stereotyped lack of co-ordination between arteriole and capillary in the vasa vasorum of the involved extracranial vessels.

A most extensive investigation of the so-called vasomotor neuroses or dysfunctions has been made by Müller.[69] In many of these conditions including the allergic states, such as urticaria, vasomotor rhinitis, asthma, angioneurotic edema and the like, he found the same typical picture in the peripheral vascular bed. He termed the arteriolar constriction with capillary dilatation "the spastic atonic state," and noted, as other observers have done, that not all tissue areas were involved, but that areas of arteriolar and capillary dysfunction would alternate with normal areas. He pointed out that the anoxia in the involved tissue would lead to increased capillary permeability.

Brown[18] observed destruction of the leukocytes in the involved capillary loops. Code[27] has shown that most of the histamine in the body of a human being is contained in the leukocytes. Destruction

of the leukocytes in the capillary loop together with more or less injury to other involved cells would result in the release of histamine which also would increase capillary permeability. Depending on the type of cell injured, other toxic substances, such as heparin, or the leukotaxine, leukocyte promoting factor, necrosin and pyrexin, as observed by Menkin[66] might be liberated. These substances could produce the same fundamental type of vascular change seen in all reactions of the organism to stress in the internal or external environment, including those found in the allergies. It has been pointed out repeatedly that allergy is primarily a vascular phenomenon. Rich and Follis,[82] for instance, found that the Arthus phenomenon could not be produced in an area devoid of blood vessels. Klinge[56] found evidence to indicate that in the pathogenesis of allergic lesions produced both clinically and in the laboratory, fibrous necrosis of the collagen fibrils is the earliest observable organic pathologic change. Similar changes in the ground substance also were observed by Rössle.[86]

The presence of this stereotyped reaction of the peripheral vascular bed has been observed in immune reactions in experimental animals. Bally[7-9] found constriction and spasm of the vessels of the rabbit's ear in histamine, peptone and anaphylactic shock. Szepsenwol and Witebsky[102] showed that three-day-old chick embryos contained Forssman's antigen and that the vessels constrict when Forssman's antiserum is applied directly. In microscopic observations on the behavior of the living blood vessels of the rabbit during anaphylaxis, Abell and Schenck[1] observed constriction of the arterioles. Wittich[119] observed the same reaction in the vessels of the chick embryo during active anaphylaxis. McMaster and Kruse,[64] on investigating the peripheral vascular reactions in anaphylaxis, found chiefly vasospasm and arrest of the circulation in sensitized mice. They found that sharply localized contractions appeared in many arteries. In those instances in which vascular spasm did not occur for a minute or two the slowing of the circulation was the most prominent feature. Cells moving in clumps separated by plasma could be seen as though they had become sticky and adherent. This latter phenomenon which they identified as sludging of the blood, was observed by Timonen and Zilliacus[103] in allergic reactions in the human being. It was their opinion that this did not result from an antigen-antibody reaction but depended on a more primitive resistance mechanism involving the reaction of the peripheral vascular bed.

The evidence appears convincing that a typical fixed, unchanging type of vascular reaction is present and is fundamental in that it is an indispensable part of the autonomic reaction to environmental stress. It also would appear reasonable to assume that in phylogenetic

development the first stress to which the organism would need to adjust itself would be physical and chemical changes in the environment. It remains to be suggested, however, how, on the basis of this stereotyped reaction of the peripheral vascular bed consisting of arteriolar constriction with atonic dilatation of the capillary and venule, we can differentiate the allergies from other types of inflammatory reaction resulting from stresses occurring in either the internal or external environment. This differentiation appears to reside in the hypothesis of autonomic dysfunction.

Hypothesis of Autonomic Dysfunction. Eppinger and Hess[36] suggested and described the hypothesis of autonomic imbalance or dysfunction. This has been restated as follows by Wenger[113] to bring it into line with more recent findings. 1. The differential chemical reactivity and the physiologic antagonism of the adrenergic and cholinergic branches of the autonomic nervous system permit a situation in which the action of one branch may predominate over that of the other. This predominance or autonomic imbalance may be phasic or chronic, and may obtain for either the adrenergic or the cholinergic system.

2. Autonomic imbalance when measured in an unselected group of persons will be distributed continuously about a central tendency which shall be defined as autonomic balance.

The Role of Autonomic Dysfunction in Allergy. Kuntz[58] pointed out that some of the most characteristic manifestations of allergic disease are causally related to heightened parasympathetic or cholinergic activity. He was of the opinion that the so-called allergic state could not exist in the presence of a normal functional status of the autonomic nerves. It seemed to him that abnormal functional states of the autonomic nerves might be induced by the tissue reactions to the sensitizing agents in question, but on the other hand not infrequently the modified functional status of the autonomic system is a factor in the etiology of allergic disease. He stated that although many allergic manifestations undoubtedly result from the antigen-antibody reaction of the tissue elements, the manifestations of physical allergy cannot be explained on this basis. In either case, however, Kuntz noted that the functional disturbances bear essentially the same relationship to the autonomic nerves. These functional disturbances involve primarily tonic changes in the musculature of the visceral organs and especially in the vascular system. The cholinergic influence in allergic reactions of all types is indicated by the fact that regardless of which tissue is affected, adrenin affords relief. The general adrenergic reaction tends to counteract

the effect of the local cholinergic stimulation wherever the disturbance may be.

Kennedy[53] also pointed out the importance of the autonomic system in allergic reactions. He observed that a sensitized person may exhibit allergic phenomena on emotion only when the autonomic system is triggered by such emotion and at the same time is in a reactive state. He felt that in time a system-habit reaction, referable to an unstable autonomic mechanism, might develop in such individuals. In migraine, he noticed the presence of arteriolar spasm with atony of the capillary and venule to be preponderantly on the same side of the body as the headache which he felt was on the basis of localized intracranial edema secondary to increased capillary permeability.

Belák[13] presented evidence which suggested that the production of immune substances took place secondarily to an autonomic reaction. This would suggest that the reaction of the peripheral vascular bed which is an integral part of any autonomic reaction probably preceded in phylogenetic development the appearance of an antigen-antibody reaction.

In summarizing his own work and that of his associates Belák classified immune substances in relation to the autonomic nerves as follows:

1. Sympathergic immune substances are the essential nonspecific antibodies, such as the alexins, opsonins and complement which are always present. He found their production to be increased by sympathetic stimulation and inhibited by parasympathetic stimulation.

2. Parasympathergic immune substances are the essential specific antibodies, such as antitoxin, precipitin, agglutinin and lysine. He found that the production of these substances is augmented by parasympathetic stimulation.

Kuntz[58] concluded that undoubtedly the specific immune substances are related to cholinergic nerves both of sympathetic and parasympathetic origin and that they respond to cholinergic (parasympathetic) stimulation according to a common mode.

Halphen and Maduro,[39] in studying spasmodic coryza, stated that when an attack of vasomotor rhinitis is produced by contact with an allergen, the allergen is unable to produce symptoms unless the individual has a pre-existing functional disorder of the autonomic system. They considered that cold, humidity, physical fac-

tors such as sunlight on skin surfaces and tobacco fumes certainly could produce vasomotor coryza solely by an autonomic mechanism. They were of the opinion that either local or general intolerance was fundamentally only the reflection of an acquired or hereditary autonomic dysfunction. That this is oversimplification of the problem is suggested by the circumscribed area of the lesions of allergy. White and Smithwick,[115] Kuntz[58] and others have pointed out that the cholinergic fibers are the ones giving a localized discharge of stimuli.

In his hypothesis of the general adaptation syndrome Selye[95] suggested that environmental stress of all types called up a series of interrelated nonspecific systemic reactions of the body, the purpose of which is restoration of physiologic equilibrium. These reactions consist of physicochemical changes in the tissue fluids, reactions of the peripheral vascular bed and especially hormonal reactions. He pointed out that a review of the literature indicated the controlling position of hormones of the anterior pituitary and adrenal cortex in that such resistance reactions could not take place in the absence of the adrenal cortex or the anterior pituitary.

These reactions did not require an antigen-antibody mechanism for their completion. Selye[95] was struck by the observation that these reactions were invariably the same no matter what stimulus called them forth. The alarming stimuli which Selye found capable of initiating the general adaptation mechanism are essentially the same as those previously described by Cannon[20] in his hypothesis of homeostasis, by Petersen[75] in his hypothesis of autonomic disintegration and by Duke[33] in his hypothesis of physical allergy. Selye noted particularly that resistance could be developed to specific environmental stimuli without the mediation of an antigen-antibody reaction. He also pointed out the destruction of lymphoid tissue that occurred during the alarm phase of the general resistance mechanism. He called attention to the work of Sabin,[91] McMaster and Hudack,[63] Dougherty, Chase and White,[25, 30] Harris and associates,[46] and Ehrich and Harris[34] which indicated that the site of antibody formation may be the lymphocyte or at least the reticulo-endothelial system. Rostenberg and Brunner[88] also critically reviewed the literature on antibody formation. They favored the hypothesis of enzymatic adaptation suggested by Burnet,[19] and stated that the somewhat divergent experimental findings might be welded together if it was considered that the primitive reticulum or undifferentiated mesenchymal cell might be the site of the enzymatic adaptation. Valentine, Craddock and Lawrence[107] have suggested that this work requires confirmation and that some of these conclusions may be erroneous. However, it can hardly be denied that this work does

suggest that a stereotyped reaction of the autonomic system takes place before an antigen-antibody mechanism develops.

Selye divided the general adaptation mechanism into three stages: the alarm reaction, the stage of resistance and the stage of exhaustion. The stage of the alarm reaction was subdivided into the stage of shock and the stage of counter shock or reaction. The stage of shock bears much resemblance to the stage of exhaustion. It seems reasonable to assume, therefore, that a defect in the autonomic mechanism which calls out the stage of counter shock which eventually leads to the stage of resistance might well be considered a fundamental part of a dysfunction of the autonomic system. The similarity of the histologic picture of shock and allergy has long been noted.[97] For this reason the reacting cells have been termed the shock organ. The great difference in the two conditions is the localized or focal part of the peripheral vascular bed involved in allergy as opposed to the generalized reaction in shock. That allergy might result from a disturbance of the anterior-pituitary, adrenal-cortical hormone also is suggested by the work of Kendall[51, 52] on the physiology of the adrenal cortex.

In discussing the relation of the adrenal glands to immunity, White[114] stated that the factors which contribute to immunity are genetic, cellular, nutritional and hormonal. He stated that evidence is available that the adrenals play a significant role in the defense against physical, emotional and noxious stimuli. In his opinion elucidation of the role of the adrenal cortex has been obscured by studies with the hormone of the adrenal medulla since epinephrine has been established as a powerful stimulator of the rate of production of hormones of the adrenal cortex. While in this paper he emphasized the role of the adrenal cortex, White[114] pointed out that the level of functioning of the adrenal cortex is markedly influenced by nutrition and by stimuli present in the environment. He favored broad use of the term immunity with a connotation of increased resistance to both nonantigenic and antigenic stimuli.

Tuft[105] recently stated that although the clinical findings of Duke have been verified repeatedly, no evidence has been presented as yet to indicate that the reactions depend on an antigen-antibody mechanism. Attempts at antibody demonstration have been generally unsuccessful. For these reasons it seemed likely to Tuft that the reactions of physical allergy are based on a physicochemical rather than an antigen-antibody mechanism. He also stated that there is no definite symptomatology or clinical picture characteristic of physical allergy by which it could be readily differentiated from antigen-antibody allergy.

It seems, therefore, that not only is allergy possible without the mediation of an antigen-antibody mechanism but that restriction of the term immunity by such an assumption of an antigen-antibody reaction may be incorrect.

The evidence presented seems to indicate definitely that the hypothesis of von Pirquet is no longer adequate as a working hypothesis because too many conditions recognized clinically as allergy fail to meet the criteria established by it. It is felt that a more adequate working hypothesis has been established by search of the available evidence. This evidence indicates that the peripheral vascular components of an autonomic reaction are the fundamental factor in the reactions by which the body attempts to restore physiologic equilibrium when subjected to environmental stress of any type. Allergy occurs when localized hyperactivity of this primitive immune reaction, with a cholinergic preponderance, develops. Consideration of allergy as a result of a dysfunctional preponderance of the cholinergic portion of the autonomic system seems to fit the available evidence better. Since the hormonal system is an integral part of the autonomic system as defined by Petersen,[75] along with the physicochemical reactions at the semipermeable membranes and in the tissue fluids, and the autonomic nervous system, the hormones of the anterior pituitary and of the adrenal cortex would be included.

There seems to be no particular reason for abandoning von Pirquet's term, "allergie" however. Its retention to cover the conditions empirically diagnosed as allergies would serve to retain in our memory his great contribution to the study of immunologic mechanisms. An attempt to replace it with another word might add to the confusion produced by the tendency to give different names to identical physiologic processes on which Harley[44] commented adversely.

Kahn[50] has defined an allergic individual (1) as one who may react maximally to stimuli that would produce only a mild autonomic response in a normal person, (2) as one who has a tendency to react to stimuli which would not develop a tendency to reaction in a normal person and (3) as one who reacts to lesser stimuli than would provoke a similar reaction in a normal person.

Stiles and Johnston,[98] Baajol and associates,[6] Brown[18] and Müller[69] have presented evidence that this tendency to develop abnormal reaction to environmental stimuli is inherited.

Duke[33] has pointed out that a reflex type of allergic reaction may involve an area, a tissue or an organ. Petersen has spoken of "focal" autonomic dysfunctions.

A NEW WORKING HYPOTHESIS

Allergy may be defined, therefore, as an inherited predisposition to a localized type of autonomic dysfunction mediated by cholinergic fibers of the autonomic system. In these localized areas a stereotyped reaction of the peripheral vascular bed occurs consisting of arteriolar spasm with atonic dilatation of the capillaries and venules. This picture produced only by a maximal stimulus in a normal individual may occur in certain tissues and organs of an allergic individual in response to a normally minor stimulus. This reaction also may take place as a result of environmental exposure to stimuli to which a normal individual would not develop a reaction. The same degree of reaction may occur in an allergic individual in response to a much less severe stimulus than would be required to produce it in a normal individual. These reactions result in a greater or lesser degree of cellular damage and the release of histamine and other toxic substances depending on the type of cell injured.

The clinical picture of allergy may be produced by reaction of the peripheral vascular bed resulting in the production of anoxic capillary loops which may lead to typical allergic edema or necrosis and be classified empirically and clinically as allergy.

An antigen-antibody reaction may be associated with the vascular reaction and may aid in damaging the cell, but it is a secondary phenomenon, phylogenetically more recent than the vascular component of the autonomic reaction. This definition of allergy includes all types of allergy and yet serves to differentiate clearly allergic and nonallergic processes.

I[117] have considered this focal type of autonomic dysfunction in a previous paper. The fundamental assumption was that allergy is a clinical phenomenon. The diagnosis of allergy is primarily made empirically by observation of a gross lesion and of changes occurring in the function of organs and tissue in the light of past clinical experience. Observation may be extended secondarily by microscopic and immunologic methods. This is the manner in which the diagnosis of allergy has always been made, but it is inconsistent with a strict adherence to the hypothesis of von Pirquet.

Since von Pirquet and later Kahn (hyperimmunity) insisted that allergy is altered reactivity, it should be possible to discover the normal prototype from which in each instance allergy has diverged. It would seem reasonable, therefore, to speak of three related but not identical types of allergy: (1) physical allergy; (2) bacterial or tissue allergy, and (3) humoral allergy.

In physical allergy no antigen-antibody mechanism is present, cellular injury and the typical clinical picture being produced by anoxia. Its normal physiologic prototype can be considered the alarm reaction of Selye.

In bacterial or tissue allergy the fundamental autonomic (vascular) defense mechanism is retained but it is suggested that in the process of phylogenetic development this defense mechanism has been supplemented by the development of protective antibodies. These protective antibodies are primarily attached to certain tissue cells, but circulating antibodies may occur as a sort of by-product of cellular immunity as suggested by Canon. The normal prototype of tissue allergy could be considered to be granulomatous inflammation.

In humoral allergy, although antibodies are attached to cells, humoral or circulating antibodies are the outstanding feature. These may be the "blocking" univalent antibody described by Cooke and associates[28] and Loveless.[62] It would appear that circulating antibodies take up some of the impact of the invading antigen so that less severe tissue injury is produced in the host. The normal protoype of humoral allergy could be considered to be suppurative inflammation.

There is nothing in this concept of allergy to suggest that these three types of allergy are mutually exclusive. For instance, perennial vasomotor coryza which appears to be on the basis of a physical allergy may be frequently observed, especially in the cold months, and yet have seasonal exacerbations that appear to be on the basis of a specific sensitivity to pollen.

The working hypothesis of allergy as a type of autonomic dysfunction suggests the gradual growth in the animal organism of an increasingly more elaborate defense mechanism and that the new developments are added to the primitive stereotype autonomic defense mechanism rather than replace it. The concept of allergy as primarily a hyperfunction or dysfunction of this stereotyped mechanism does not appear to be in conflict with any of the observed facts. It explains the gradual, rather than the abrupt, transition from one type to the other and why there may be a mingling of types. It also explains why, since the circulating antibody would appear to be a later phylogenetic development, it is not possible to discover evidence of circulating or sensitizing antibodies in so many patients with clinical allergies, nor to give them symptomatic relief by hyposensitization through the medium of the injection of specific antigens. Duke[33] pointed out that in the majority of allergic individuals the reaction is not to a type of chemical stimulus (protein)

that could reasonably be expected to result in antibody formation. At present there are several disorders such as Ménière's disease and myalgia in which the decision has not been made as to whether they were really allergic or not. With the present hypothesis of autonomic imbalance as a basis of allergy these disorders are readily classified as allergic, and successful treatment on a logical basis can be planned. This hypothesis throws the emphasis on the medical and psychosomatic aspect of the treatment of allergy which is receiving increasing consideration, as opposed to the strictly immunologic aspect.

THE MEDICAL TREATMENT OF ALLERGY

The advantage to be gained by consideration of allergy in the light of autonomic dysfunction is that all the allergies, whether an antigen-antibody reaction is present or not, can be treated from the viewpoint of clinical medicine. Moreover, one type of treatment need not exclude others.

The effect of nonspecific stress such as inadequate nutrition, inadequate rest, inadequate amusement and relaxation in lowering the threshold of allergic reaction has long been known, but it has not been featured in allergic treatment because of a seeming reluctance to employ any but immunologic methods. The effects of physical agents in producing allergic reaction have been decried and there has been a tendency to deny them a place in allergy because immunologic treatment accomplished little.

Vasodilators. The vasodilators, however, have been known for a long time to produce favorable effects in physical allergy. The traditional form of attack on many of the allergies has been by vasodilatation. Many of these conditions were treated by the application of heat before any concept of allergy had been formulated. The treatment of vasomotor rhinitis and the vasomotor stage of the common cold by the hot mustard bath and by the opiates preceded the use of the antihistaminics by a considerable period.

Since the principal functional lesion in allergy appears to be vasospasm affecting the arteriole, an attempt to correct this dysfunction would appear to be the most logical approach.

The use of vasodilators for treatment of the allergies is based on the supposition that a vasodilator will release the spasm of the arteriole, resulting in renewed blood flow through the capillary loop which sweeps the contained cellular detritus and released toxic substances into the general circulation where they are immediately metabolized.

Duggan[32] has indicated that many of the vasomotor disorders affecting the eye, both those thought to be allergic and those not, are on the basis of arteriolar spasm. He has furnished a thorough review of the literature and added many suggestions in relation to the treatment of disease affecting the eye and its adnexa by vasodilatation.

Papaverine was one of the earliest vasodilators suggested for use in Ménière's disease by Müller. Diehl[31] suggested its use in the common cold. Russek and Zohman[90] have found papaverine useful in the relief of cerebral angiospasm. Eppinger and Hess[36] in 1914 were among the first to suggest use of the vasodilator histamine for vasomotor neuroses such as angioneurotic edema. Müller recommended it for similar conditions in 1922 and Kling[55] in 1934 advised its use for rheumatic affections because of the effect as a vasodilator. Horton and his collaborators[48, 49, 96] have found histamine effective in the treatment of urticaria and Ménière's disease.

Weiss, Robb and Ellis[112] showed that histamine produced marked vasodilatation of the intracranial vessels of most individuals. These findings were confirmed by Wakim and his associates.[110]

The therapeutic effect of histamine on the allergies is the relief of vasospasm; its action is not essentially different from that of any other similarly acting vasodilator.

Harris and Moore[45] were the first to suggest the use of nicotinic acid for Ménière's disease. Bean and Spies[10] found that nicotinic acid, and all of its pyridine compounds which contained the free nicotinic acid radical were vasodilators. Popkin[78] and Abramson, Katzenstein and Senior,[2] Crino and Lenzi[29] and Malaguzzi Valerie and Paterno[65] observed the effects of nicotinic acid to be similar to those of histamine. Roniacol (3-pyridine methanol), which is stated to be converted in the organism to nicotinic acid, is a long-acting vasodilator that can be given by mouth and has been found effective in the treatment of the allergies. Wakim and associates[109] found priscol (2-benzyl-4, 5-imidazoline hydrochloride) to be an effective vasodilator and it has been used in the allergies with success.

Sympathomimetic Drugs. The fact that cholinergic nerves are concerned in the production of the allergies suggests that a beneficial effect should be obtainable by drugs which stimulate the adrenergic or paralyze the cholinergic system.

White and Smithwick[115] classified the neurohormones and the most potent drugs which act on the sympathetic nerves as follows: Of the drugs acting on the sympathetic nerves, those which produce

a stimulating effect are epinephrine or adrenalin, sympathin, ephedrine and amphetamine sulfate; those which produce a depressing effect are ergotoxine and nicotine. Of the drugs acting on the parasympathetic nerves, those which have a stimulating effect are acetylcholine and pilocarpine; those which are depressing are atropine and nicotine.

The advisability of prohibiting the use of tobacco in the allergies has long been debated. The studies of Roth[89] indicate that smoking promotes vasospasm. Use of tobacco in allergy, therefore, appears contraindicated.

Atropine and epinephrine have long been found useful in the allergies as have ephedrine and amphetamine.

Extracellular Fluid. Because the typical allergic wheal or edema is produced primarily by increased capillary permeability with the consequent formation of an area of extracellular fluid collection, drugs acting to decrease capillary permeability and to get rid of extracellular fluid have been found useful in the medical treatment of the allergies. Allergic edema has been shown by Rössle[86] to differ from cardiac edema only in its increased content of serum proteins. Schemm[93] found that extracellular edema in cardiac failure could be relieved by the elimination of sodium. Therefore, a low salt diet and diuretics have been found useful in treatment of the allergies both by Stoesser and Cook[99, 100] and Kern.[54]

The Effect of Relative Acidity. Kuntz[58] stated that changes in the autonomic functional balance associated with changes in the acid-base balance have been amply demonstrated. Consequently restoration of the autonomic balance by appropriate therapeutic measures designed to restore the acid-base balance should not be regarded as beyond the range of possibility in allergic disease.

Alden,[3] Beckman,[11] Roberts[85] and others have reported success in the treatment of allergic disease by the use of acidifying agents to reduce the potential alkalosis.

Selye also advocated the use of acidifying salts in disorders apparently provoked by an excess of the salt active corticoids as opposed to the sugar active corticoids such as the compound E (cortisone) of Kendall. In Ménière's disease ammonium chloride in enteric-coated capsules containing 0.5 gm 4 to 6 capsules being given during meals three times a day, appears to be useful when combined with vasodilator therapy.

Ascorbic Acid. It is suggested that in some individuals allergic reactions are produced by a relative depletion of the adrenal cortical

hormones. That this may be owing to the lack of ascorbic acid, the precursor of corticoid hormone, is indicated by the fact that ascorbic acid has been reported to be effective in relieving the symptoms of allergy in some individuals. Ascorbic acid also has a direct effect on capillary permeability, its lack being associated with increased permeability and fragility of the capillary wall.

Vitamin P. These substances have been found necessary to complement the local action of ascorbic acid. The absence of both ascorbic acid and Vitamin P appears necessary to produce the symptoms of scurvy. Beiler and Martin[12] found that in the presence of ascorbic acid, compounds having a Vitamin P activity manifest a well-marked inhibitory action on hyaluronidase. These authors were unable to demonstrate whether this action was a direct inhibition of hyaluronidase by ascorbic acid or was due to a potentiation of Vitamin P by this substance.

I have found the combination of ascorbic acid and rutin effective in certain manifestations of allergy, especially as a maintenance therapy to be taken after the acute symptoms of the disorder have been relieved by other medication. In my hands 250 mg of both rutin and ascorbic acid taken three times a day tends to prevent the return of allergic symptoms. Saylor[92] recently has reported the effective treatment of allergic vasomotor rhinitis with hesperidin chalcone sodium.

Vitamin Therapy. Selfridge[94] has emphasized particularly the effect of the vitamins of the Vitamin B complex on lipoid metabolism and vascular function. I have given vitamin therapy a trial but I have rarely found evidence of a marked change in a patient's symptoms or signs following vitamin therapy.

Fatty Acids. Hansen[43] has shown that lack of unsaturated fatty acids in the diet may lead to allergic conditions. Hansen found that certain infants with eczema were materially benefited when fats such as lard, corn oil and raw linseed oil were added to the diet.

I have observed marked relief to symptoms of vasomotor coryza in children who refused to eat the fat of the meats served, by the feeding of the fats recommended by Hansen.

Specific Allergy Therapy. A carefully taken history will often reveal more clinically useful information in regard to foods, contacts and the like than skin tests. In pollinosis and inhalant allergies in general, useful clinical information may often be gained by skin testing. When clinically significant positive results to skin tests are obtained, attempts at hyposensitization are frequently beneficial. I

have found, however, that supplementary medical treatment will often hasten and increase the symptomatic improvement even of patients who appear to be receiving clinical benefit from so-called specific therapy. The details of successful specific management of the allergies forms a literature in itself and will not be considered here. Possibly the best outlines of treatment from the immunologic viewpoint for conditions in the ear, nose and throat are those furnished by Ashley,[5] Hansel,[40, 42] Black[15] and Rawlins.[80]

SUMMARY

A theory of allergy based on the autonomic vascular reactions is felt to furnish a better working hypothesis from the standpoint of clinical diagnosis and treatment than one based on the antigen-antibody concept. At present the diagnosis of allergy is made clinically and positive reactions to skin tests merely give confirmatory evidence of allergy. In many such individuals positive skin reactions cannot be obtained. In the entire group, however, it is possible to obtain confirmatory evidence of allergy by studyin the capillary bed by biomicroscopy. Treatment by specific methods leaves much to be desired. Supplementary treatment by nonspecific methods will often produce a favorable clinical result unobtainable by specific methods alone. There is evidence that the typical histologic picture of allergy may occur without the intervention of an antigen-antibody mechanism. A concept of allergy as localized or focal autonomic dysfunction is far more consistent with clinical practice than the antigen-antibody concept; it opens up new avenues of therapeutic approach to the allergies and offers greater hope of symptomatic improvement to a patient who has one of the allergies.

MAYO CLINIC.

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XI

NOSE AND THROAT TREATMENT IN THE PREVENTION OF COLDS

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Over twenty years' study of both prevention and treatment of colds on the Student Health Service at the University of California has served to illuminate many of the problems arising from abnormalities in the nose, throat, sinuses, bronchial tubes, or lungs, particularly as related to susceptibility to colds.

This paper is based upon a study of 2667 University of California students, with the purpose in mind of discovering the frequency of abnormal conditions in the respiratory tract, especially the importance of nose and sinus conditions in relation to the special problem of alleviating susceptibility to colds. In every one of the 2667 students the local examination was made by a nose and throat specialist. At the same time, each student had the benefit of a complete general physical examination, chest x-ray or fluorogram, urinalysis, Wasserman, and often a tuberculin test. The services of an experienced allergist (Dr. Albert Rowe) and a lung specialist (Dr. James Harkness) were available when the findings indicated associated problems in these departments.

With the aid of the nose and throat specialist, 1106 abnormalities of sufficient degree to be possible adverse influences upon defense capacity against colds and chronic local infections, especially in the sinuses, were noted in the 2667 University of California students (see Chart 1). Thus, it was necessary to consider these factors in nearly half of our cases (44%), and, recognizing their presence, to judge whether their remedy would benefit defense against acute and chronic respiratory infections and irritations.

Estimation of hereditary natural resistance gives a clue as to whether local treatment in the nose or sinuses is indicated at all, and, if indicated, whether it may be sufficient alone, or will have to be combined with general measures in order to insure a successful result. As shown in a previous study, the natural (corpuscle-antibody) defense mechanism of the human body varies along hereditary lines

from zero to perfect, and its efficiency can be judged fairly accurately by the experience of the individual with infections over a period of years (in the case of our students from 0 to entering college at 18 years).

Thus, in the same environment a student who has come up to college through the public schools and hasn't had any infections whatever, not even measles, and never a cold, certainly has an excellent automatic resistance apparatus.

CHART 1.

Total number of students studied		2667
Total number of abnormalities noted by specialist		1106
Spurs	106	
Deviated septum, enough to obstruct	370	
Chronic rhinitis, polyps, thickened membranes	179	
History sinusitis and present on examination	451	
	1106	

On the other hand, the student in the majority group who has had the usual children's diseases, perhaps one severe illness like scarlet fever, influenza, etc., and two or three colds a year, may be classed as having average natural resistance.

Finally, there is the "susceptible" with poor natural resistance, who may have had everything on the list, ear abscess, mastoiditis, pneumonia, and experiences as many as a dozen or two infectious colds each year. Separation of the patients into the three groups of good, average, and poor natural resistance, provides a practical way to approach the problem of resistance to colds.

GOOD NATURAL RESISTANCE GROUP

In our group of 1106 students showing defects in the nose or sinuses of a sufficient degree to constitute an adverse factor in defense agains colds and chronic local infections, 206 had estimated good to excellent natural resistance. The great majority of these exhibited no infection in noses with septum bent to the point of complete obstruction, were happily unaware of large spurs that all but closed the airway on one side or the other, were not discommoded by old fractures that messed up the entire nasal apparatus, apparently, because of their exceptional inherited defense capacity could

prevent pathogenic bacteria, viruses, etc., from taking advantage even of these unusually great aids to colonization.

A case history of a student with good natural resistance, and hence no colds even with the nasal septum bent to the point of obstruction, well illustrates this group.

Case No. 1.—George W., age 18, a city dweller always, had had chicken-pox at nine years, whooping cough at nine years, appendectomy at fifteen years, and never had a cold. Since he had not had the usual measles and mumps, in addition to chickenpox and whooping cough and no influenza he was classified as having better than average natural resistance to infections.

The family history showed both parents living and well, and no history of tuberculosis anywhere in the family.

Physical examination showed medium development and average condition. General examination was quite normal, i.e. heart, lungs, abdomen, genitalia, and extremities all normal. In temperament he was found to be excitable with blood pressure to 157/80 and pulse 130 under the stress of examination, but pulse and blood pressure normal when at ease; i.e. not fixed above average, vessels elastic, heart undamaged, and kidneys normal.

Specialists' reports were as follows: Nose and thoat: August 29, 1936—Nose shows deviated septum, membrane normal. No sinusitis, tonsils normal, no adenoids. March 15, 1940—Review by nose and throat physician, while searching for a focus of infection possibly influencing a painful heel. Nose—right side nearly completely occluded by deviated septum. Mouth—teeth appear O.K. Tonsils—normal, not inflamed, no pus expressed. Transillumination—M. & F. clear.

Laboratory Tests: Uurine normal. Kline negative.

X-rays: Complete denture and lower left jaw—no abscess formation. Minute areas of caries.

Cold Record at the University of California: In addition to the history of no colds (in spite of a marked nasal defect), this student was observed by us over a period of six years and actually had no colds during this time. The record shows 53 separate observations during these years, i.e. general examination, blood pressure readings, treatment of cuts, bruises, athletic injuries, etc., but no colds reported or observed. It is reasonable to conclude that his defense apparatus was sufficiently good to keep out infections, both acute and chronic, in spite of an obstruction from a deviated septum, sufficient to favor

colonization not only by the more virulent infections that pass through the community, but also by the ever present low grade invaders found in every nose, and causing both acute and chronic inflammation in others of less perfect defense capacity.

Accepting the dictum that no treatment of a nasal defect is demanded if the natural resistance of the individual is sufficient to keep out all infections in spite of the abnormality, it is equally true that remedy should be applied, even in those of estimated good natural resistance, if the abnormality is of sufficient degree to open the way to repeated acute or long drawn out chronic infections. Benefit from remedial action proves this point as the following case history indicates:

CASE NO. 2.—Henry K., Jr., age 17, had lived in suburbs ten years and within a city seven years, thus being exposed to prevailing infections in crowded city schools. In spite of this, his record showed only measles at seven years and a hip abscess at twelve years, no bone damage. As he hadn't had the usual chickenpox, mumps, and whooping cough, and no serious illness, he was classed as having better than average, in fact good natural resistance. On the other hand he gave a history of frequent colds all his life, always starting in the head.

The family history disclosed both parents living and well, with no tuberculosis, or allergy anywhere in the family, including the patient.

General Physical Examination was normal throughout. Development was medium, condition average, heart, blood pressure, abdomen, genitalia, and extremities all normal.

Laboratory Tests showed Tuberculin negative. Kline negative. Urine repeatedly showed a trace of albumin, otherwise normal.

Specialists' Reports: Nose and throat: January 19, 1940—Marked deviation of the septum. No sinusitis at the moment, tonsil tags present R & L, no adenoids. January 30, 1940—Review by medical and nose and throat departments because of albuminuria and frequent colds. The nose and throat specialist noted "complete nasal obstruction on the right and anterior tip of nose to left due to deviated septum. Large tonsil tag on right, also on left." March 13, 1940—Examination by Dr. Milton Shutes, Chief of Staff: "Right nostril completely blocked by septum to right." Operation scheduled. March 29-April 4, 1940—in hospital. Submucous resection done. April 8, 1940—Nose and throat department reports septum healing nicely. April 15, 1940—Healed.

Subsequent cold history: The operation proved to be a complete success. Our observation, covering the entire year following operation on the nose, i.e. from March, 1940, to March, 1941, (fifteen separate observations during the year) disclosed no colds reported or observed. Thus, an individual of estimated good natural resistance, but subject to frequent colds always starting in the nose where there was complete obstruction by a bent septum, was completely relieved of susceptibility to colds by repair of the nasal septum. It is fair to conclude that local operation on the nose should be done even in those of good to perfect natural resistance to infections, when the evidence indicates that the local abnormality (in this instance an obstructing bent septum) is lowering defense capacity to the point where repeated acute, or chronic infection, can get a foothold.

AVERAGE NATURAL RESISTANCE GROUP

In the group of 1106 students discovered to have nasal defects of possible consequence in regard to susceptibility to colds, 548 were estimated as having average natural resistance by inheritance; i.e. the usual children's diseases and perhaps one severe illness in the first 18 years plus two or three colds a year. Definite indications for treatment of nose and sinus conditions were considered present in this majority group where the abnormality obviously lowered resistance to prevailing acute respiratory infections, or prolonged the process of getting rid of a long established infection. However, as many in this group "dried up" their sinus infections, or attained a degree of defense that kept out new infections by means of a course of mixed respiratory bacterial cold vaccine, by improving their general condition, by learning to avoid unnecessary contaminations, or by controlling an allergy, etc., as were improved by local treatment of nose or throat.

Thus in the treatment of nose and sinus abnormalities in individuals of estimated average natural resistance, the physician attempting to set up a defense against colds often has to solve a problem requiring the rarest of judgment. Since the indications for local treatment are not imperative in this group, the physician will find it more practical to try what can be accomplished by general measures first, and resort to local treatment or operation by the specialist if the nasal or sinus infection persists, or if repeated new infections occur in spite of general treatment. At the same time the physician must recognize that in the average resistance group, as in the group having good to excellent natural resistance to colds, there are instances where the local treatment alone will be sufficient to relieve susceptibility to colds. A case history from our private practice group illustrates this point.

CASE No. 3.—Mr. E. E., age 49. He was classed as having average natural resistance because he had had all the usual children's diseases and many colds. However, he had never experienced a severe illness, particularly any serious complications of colds, such as otitis media, mastoiditis, or pneumonia. So he could not be placed in the poor natural resistance group even though the colds were frequent, severe, and prolonged all through childhood and up into adult life.

At 29 years of age, examination by a nose and throat specialist disclosed a marked septal deviation which blocked the airway, and prevented drainage from the sinuses. Operative repair was done, and following an uneventful recovery he has been entirely free of colds for twenty subsequent years.

Physical Examination: February 2, 1942, showed a well developed man of 49 years, in good physical condition. There was a slight excess of fat, and some patches of dermatitis on the legs, which along with a slow pulse (64-66) suggested mild hypothyroidism. No signs of allergy were found in the nose, which was bent to the left, but the postoperative airway was good, tonsils were present and normal, no evidence of irritation or discharge in the postnasal region. Heart, lungs, abdomen, genitalia were normal.

Urine normal. Blood normal. Stool normal. Fasting blood sugar 102 mg %. B.M.R. -9.

We have now observed this patient for eight years (since 1942) for routine physical examination, minor complaints, etc., and he has remained free of colds during this interval, as well as the reported twenty years following his septum operation. Thus, we have the first twenty-nine years of his life plagued by frequent colds balanced by twenty-eight succeeding years of complete freedom from colds, subsequent to a single therapeutic procedure, a local treatment (septum repair) by a nose and throat specialist, without aid of any general medical measures.

Though local treatment does suffice to end colds in some cases in the average natural resistance group, and a single general medical procedure such as a course of cold vaccine, regular sun bathing, improvement in diet, increase in rest, administration of thyroid extract, etc. may do the trick in other cases, really spectacular results and a high percentage of success in overcoming susceptibility to colds in this group demands combined local and general treatment. In every case, examination by a nose and throat specialist, as well as a complete general examination and laboratory tests, often with an opinion by the allergist, or occasionally even by the lung specialist,

should precede treatment by either the physician, the nose and throat specialist, or both together. In this way, the entirely different problems of each individual become evident, and a better prospect of success in treatment results from the preliminary survey disclosing which of several therapeutic measures will have to be applied at one and the same time. Since those of an estimated average natural resistance comprise by far the greater group, it is obvious that success in the prevention of colds always demands both a preliminary survey and a careful exercise of judgment before starting combined treatment (general medical, nose and throat, often an allergist, and occasionally a lung specialist).

POOR NATURAL RESISTANCE GROUP

In the group of 1106 students with nose and sinus defects, 352 were estimated as having poor natural resistance, i.e. history of many infections, including severe complications such as pneumonia, otitis media, mastoiditis, etc., and many more colds than the average of two or three a year, usually having every infectious cold that goes through the community.

In this group of "susceptibles" we find the absolute indications for local nose and throat treatment, even radical surgery, since a single abnormality in these may be of sufficient importance, unremedied, to block a successful defense against prevailing acute respiratory infections, as well as chronic low-grade sinusitis, etc., even if all other factors are taken care of through general measures.

On the other hand, local nose and throat treatment alone in those of very poor natural resistance to infections, however well done, usually is doomed to failure, because nullified by multiple factors other than the local nose and throat condition. Invariably multiple factors will be found to be depressing the defense in "susceptibles" and all require remedy, along with the local treatment, if any measure of success is to be had in defending these individuals against colds. Thus, in our experience, failure to protect against colds will result if the local nose and throat condition is remedied, without any attempt to improve antibody defense (prolonged course vaccines), general condition (rest, sunlight, diet increase, etc.) hypothyroidism (nearly always present in "susceptibles"), asepsis (avoid unnecessary droplet infection, stay out of infected school, business, and social atmospheres), and in fact all known factors which adversely influence defense against colds. "Susceptibles" are certain upon investigation to be found pushed down in their defense against colds by most, if not all, of the fourteen known factors that influence defense, so that combined nose and throat, general medical, allergy,

and even lung specialist care will be imperative, if they are to achieve even a modest improvement in their lifetime defense against colds.

Numerous examples can be cited of failure to achieve either temporary or long continued freedom from colds when the treatment was limited to local nose and throat care, general medical care, allergy treatment, etc. However, an illustrative case, showing benefit from combined treatment, provides the necessary emphasis regarding what is required for success in preventing colds in those of poor natural resistance.

CASE NO. 4.—Mr. Trygve B. A., age 28. This patient was classified as having poor natural resistance because, in addition to the usual children's diseases, he had been subject always to frequent and severe colds, with prolonged sinusitis, laryngitis, bronchitis, etc. He had averaged five or six severe colds each year, often was in the hospital with "flu" or other causes for high fever and prostrating illnesses, and always was undergoing prolonged courses of treatment, usually of the local nose and throat variety.

Family History: The father had been killed in an accident, the mother was living and well. There was no history of tuberculosis or allergy in the family.

General Physical Examination: In January, 1937, upon entrance to the University, routine physical examination was normal, except for scars from operative removal of renal stones. Heart, blood pressure, lungs, abdomen, genitalia, and extremities all were normal.

Specialist's Examination: Nose and throat department, in January, 1937, when no cold was present, found nose normal, i.e. no obstruction, no polyps, etc. No adenoids. No sinusitis. Tonsils "Path."

In March 1937, after winter colds had stirred up some sinusitis, the E. N. T. Department, by transillumination found the right antrum cloudy.

Laboratory Tests: Tuberculin test on January 22, 1937, P.P.D. No. 1 Positive. Urine routine in 1937 and again August 28, 1939, normal throughout. Sputum: December 22, 1939, while in hospital because of a severe cold was negative for tuberculosis. Smears for V.A.: December 21, 1939. Throat negative. Gums 10-20 fusiforms, no spirochaetes. Blood: September 2, 1938. Kline, negative. Kahn, negative. Wassermann, negative.

X-ray Examination: Chest Fluoroscopy January 29, 1937. Calcified parenchymal lesions. No evidence of activity.

Lung X-rays: October 12, 1938. No evidence of an active lesion in the lungs. Mild root gland calcification.

Sinus X-rays: December 11, 1939. No definite evidence of infection in sinuses. Pulpless teeth should be examined.

Teeth X-rays: December 22, 1939. Two large abscesses and two other pulpless teeth, probably with periapical infection. Large pyorrheal pocket between upper right lateral incisor and 1st bicuspid.

Our own observations during the first four years of this student's University life bore out the contention that he had poor natural resistance to colds. Aside from many moderate colds, the record shows that he was in the hospital in March, 1937, with temperature to 101.4° F. and a diagnosis of upper respiratory infection. Through October and November of 1937, he was treated in the E. N. T. Department for complications of rhinitis. In 1938 he was treated all through January in the E. N. T. Department for sinusitis, laryngitis, and bronchitis, finally being given a single one-half cc shot of I-V vaccine. In May he received treatment in the E. N. T. Department for pharyngitis. In 1939 he was in the hospital December 8 to 13 with a temperature of 100° F. and a diagnosis of upper respiratory infection. Again, later in December, i.e. he was in the hospital with another cold severe enough to prostrate him, the temperature going to 101° F. and the diagnosis again being upper respiratory infection.

In January, 1940, he was treated in the E. N. T. Department for acute tonsillitis, in April, for a cold with sinusitis, and in September, for sinusitis with much nasal discharge and pain in the cheeks.

During these four years the patient was treated entirely by nose and throat specialists, except when in the hospital, at which times the medical staff provided the care for the acute illness of the moment, without consideration of the general problem of susceptibility to colds, and without a coordinated follow-up on the return of the student to the Out-patient Department. However, in September, 1940, when the sinusitis became very troublesome and resistant to prolonged local nose and throat treatment, a general overhauling by the Medical Out-patient Department was ordered, and a combined assault on the problem of low resistance to prevailing acute respiratory infections was organized.

Medical examination on September 30, 1940, disclosed extremely poor physical condition, partially due, no doubt, to the prolonged cold with severe sinusitis, but much more so to years of overwork,

insufficient rest (especially sleep), deficient diet, deficient sunlight and outdoor life, extreme ignorance and carelessness regarding mode of contamination by the prevailing infections in the community. In fact, he was ignoring all the influences which depress natural resistance, attention to every one of which is a must for "susceptibles to colds." Admittedly it is difficult for the average student of small means, yet attempting a heavy course at the University to pay attention to his housing, food, rest, sunlight and outdoor exercise. And it certainly is impossible to avoid gross contamination by a complete set of the prevailing infections in the crowded classrooms, social and eating halls, not to mention business establishments, all of which students frequent. However, it was pointed out to this student how much time he had lost due to illness, and how his efficiency between illnesses was lowered by his manner of living. A deliberate effort was begun to improve his health and raise his resistance to the point of freedom from all colds. He agreed to give attention to rest, particularly more sleep, follow a high protective (high mineral, high vitamin, sufficient calories, high quality protein, fresh foods, etc.) diet which was supplied him, get outdoors and sun himself daily, avoid contamination (droplet and infected air) so far as reasonably possible.

In addition to the hygienic regime, an effort was made to improve his antibody defense by means of mixed bacterial cold vaccines. During October and November, 1940, he was given a course of Cutter CO. M.V.R.I. No. 4 count shots beginning with 0.1 cc. Gradually increased dosages brought him to 0.7 cc vaccine by December 2, and diminishing dosages after that to 0.5 cc at termination of the weekly shots on December 18.

Cooperating with the Nose and Throat Department, local treatment of the nose and sinuses was continued. Transillumination on September 30, 1940, again had showed the right antrum less clear than the left. Since x-rays of the sinuses the previous year had not shown anything definite, treatment had been purely medical. However, it was recalled that dental x-rays had shown several apical abscesses and a big pyorrhea pocket on the right. On the possibility that continued resistant sinusitis, centering in the right antrum might be fostered by the dental condition, a dental consultant was called in and finally in December, 1940, the abscessed teeth were removed and the pyorrhea pocket drained. It was discovered that the dental infection was invading the right antrum and definitely contributing to the resistant sinusitis.

Following combined medical, nose and throat, and dental treatment, a great improvement resulted in this patient's condition, and

whereas formerly he was having almost constant treatment for colds or prolonged complications thereof, he now became entirely well and required no treatment whatever. Our record shows no colds or sinusitis or any other complication in 1941, and through January, 1942, at which time he left the University and due to war conditions could not be followed up. Though a little over a year of complete freedom from colds or complications of colds is not a sufficient interval for absolute proof of the effectiveness of the combined treatment, the extreme contrast between this good year and the preceding bad years did indicate very real benefit from combined treatment.

SUMMARY

1. Complete medical examination, laboratory tests, x-rays, and specialists' (nose and throat, allergy, lung, dental) examination should precede treatment of susceptibles to colds, known to have local abnormalities in the nose, sinuses, etc. in order to clarify their entire problem.

2. Highest percentage of success in raising defense in susceptibles to colds results from combined treatment by medical and nose and throat specialists, often including the allergist, and even the lung and dental specialists.

3. Great convenience in deciding what therapeutic measures are applicable to the individual case results from division of the patients into three groups according to estimated natural resistance to infections, i.e. (1) good to excellent natural resistance, (2) majority having average natural resistance, and (3) "susceptibles" having poor natural resistance.

UNIVERSITY OF CALIFORNIA.

XII

DIAGNOSIS AND PROGNOSIS OF MALIGNANCY OF THE NASOPHARYNX

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It has been conclusively established that surgery has no part to play in the management of malignancy in the nasopharynx, except, of course, for the taking of biopsies to establish the diagnosis and to check the status of suspicious areas for recurrence. With the definitive therapy relegated to the province of the radiotherapist, for few of us are adequately trained or equipped for the task, we must inquire as to the part to be taken by the otolaryngologist. The mechanics of management of malignancies of the nasopharynx belong to the domain of the radiotherapist assisted by the otolaryngologist. The diagnosis and the question of prognosis are problems of concern to the otolaryngologist and, to a lesser degree, to the ophthalmologist.

To the otolaryngologist falls the task of early diagnosis. He occasionally sees the patient at a stage when the symptomatology is vague and not directing. A thorough initial examination may reveal a mass, an ulceration, or an asymmetry of the nasopharynx which require investigation. Too often a hyperactive gag reflex leaves this area unseen, or the view has been so fleeting that small lesions may be overlooked. The importance of lesions in this area is so great that the use of topical anesthetics is not uncommonly required for adequate examination. Checking the symmetry of this anatomic culde-sac may enable one to diagnose a malignancy in a curable stage. We are morally obligated to give this full measure of professional attention.

The earlier a lesion is diagnosed the better the chance of cure. It is incumbent upon the otolaryngologist to examine thoroughly each patient regardless of complaint so that he may possibly find pathology which has not yet symptomatically manifested itself. An abnormal tissue should be biopsied. It is a disservice to our charges

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if we temporize and observe an abnormal mass until a metastatic node indicates the diagnosis. One must, however, keep in mind the fact that certain masses in the nasopharynx of young males are prone to hemorrhage, and, therefore, biopsy should not be attempted as an office procedure in this group. The possibility of juvenile nasopharyngeal angiofibroma should not deter one from surgical biopsy. The age spans of benign and malignant lesions in this area overlap but the prognoses of the two are, of course, considerably different. Cancer in the nasopharynx occurs over ten times as often as juvenile angiofibroma. "The disease sometimes occurs in children and occurs more often at ages below thirty than any other malignant tumor of the head and neck. This anatomic variety of cancer is encountered more frequently in males (80%) than in females."[1]

Our routine examination of the patient should include inspection and palpation of the neck. Cervical node metastasis is most often the first evidence of malignancy in the nasopharynx. Erik Godtfredsen[2] in reporting 454 cases found that metastatic cervical nodes constituted the most frequent initial symptom. Slightly less frequent were nasal symptoms. Otologic symptoms were third on his list and ophthalmoneurologic symptoms were fourth.

The presence of cervical nodes, unilateral or bilateral, in all except young children, and we make that exception with reservations, is a definite indication for aspiration biopsy. A diagnosis of carcinoma means metastasis, and a careful search must be made for a primary lesion in areas draining into the involved node group. It is possible for a malignant lymphoma to be primary in a cervical lymphatic node, but the assumption is not justified until repeated examination and the passage of adequate time have definitely ruled out the presence of a primary lesion everywhere in the head and neck, particularly in the area of Waldeyer's ring.

Cervical nodes, nasal obstruction, deafness and cranial nerve involvement are all relatively late manifestations of the disease, and, while they should direct attention to the nasopharynx as a possible source of pathology, the chance of cure is materially less than treatment of an early lesion could achieve. It is the less directing symptoms that we must concentrate upon. Vague throat consciousness, alteration of vocal resonance, slight difficulty in swallowing, postnasal drip, and epistaxis should direct our attention to this area. The latter symptom is relatively uncommon and is usually associated with the more mature type of epidermoid carcinoma. It is not necessary to enumerate the various techniques of examination to the otolaryngologist, but it may be stated that the postnasal mirror

is the most effective instrument for the examination of the pharyngeal vault.

While benign lymphoid tissue is found in the nasopharynx of adults, no neoplastic tissue should be so labeled from clinical impression alone. Cytologic examination is necessary to prove the benign or malignant character of the tissue particularly in an area where malignant lymphomas may be present. A biopsy should be taken. In order that we may determine the value of the Papanicolaou technique or its modifications in this area, it would be well also to obtain a smear for additional examination. Such a procedure may establish an additional diagnostic aid to our armamentarium.

A diagnosis of malignancy in the nasopharynx must be correlated with the symptomatology and the roentgenographic findings so that the total extent of the lesion may be delineated for the purpose of adequate therapy. It is not unusual to find a small surface lesion associated with a relatively wide expanse of extention to the base of the skull and into the cranial cavity. Though metastases are usually limited to the cervical nodes, pulmonary involvement is next in frequency. Roentgenography of the chest and skull must precede definitive therapy. The skull films most helpful are the lateral and the axial views. The latter is the most important. In examining such a film, particular attention should be directed to the region of the foramen lacerum and the foramen ovale. It is in these directions that the disease has a great tendency to spread. These pathways result from the anatomy of the area. The pharyngeal fascia is very firmly attached to the base of the skull anterior to the foramen magnum and extends laterally to the petrous portion of the temporal bone where it surrounds and supports the eustachian tube and is continous with the fibrous tissue of the foramen lacerum. The foramina lacerum and ovale give access into the cranial cavity. Malignant lesions following the planes of the pharyngeal fascia can enter the skull close to the positions of the third, fourth, and sixth nerves, the ninth, tenth, eleventh, and twelfth nerves and the cervical sympathetic trunk. This explains the ophthalmologic and neurologic symptoms so characteristic of this disease.

It has been our experience to find that the extent of bony involvement exceeds the roentgenographic evidence of ostitic change. We must, therefore, consider the signs and symptoms to delineate the disease more completely. These signs and symptoms relate to involvement of cranial nerves either by invasion or compression. The sixth nerve is most frequently affected, but more than one may be involved, and cases have been described in which all twelve nerves and the cervical sympathetic trunk have been involved.

Once the diagnosis is established the management is shared by the otolaryngologist and the radiotherapist. While the technique of therapy is under the direction of the radiotherapist the otolaryngologist has a definite function to perform. He must indicate the position and size of the primary lesion so that the beam of radiation may be correctly focused. He must watch the mucosal reaction both for its relation to the lesion and its severity. This cooperation enables the radiotherapist to correct the scope of his field so that the entire lesion is adequately treated, and to adjust the dosage to the individual requirements of the patient. If a radium or radon pack is to be used the otolaryngologist must place it in contact with the neoplasm. The degree of cooperation between the otolaryngologist and the radiotherapist is an important factor in the success or failure of therapy. The salvage rate in malignancy of the nasopharynx varies in the reported series; the best results are obtained in the larger groups. It is possible that the better results in these reports reflect the greater experience of the therapeutic teams rather than the accidental inclusion of more responsive lesions.

Because the otolaryngologist supervises the therapy it is only natural for the patient and his family to direct inquiry as to prognosis to him. Each man has the right to put his house in order, and the physician is morally obligated to advise the patient or a responsible member of his family of the probable prognosis. This implies a more exact knowledge than can be covered by vague evasion.

Because lesions in the nasopharynx are silent until relatively late in the disease the prognosis is very poor. Only in the case of the accidental finding of malignancy during routine examination of an asymptomatic patient can one offer a guarded fair prognosis. The histology of the tumor is not too helpful, but in general the sarcomas offer a more favorable outlook than do the carcinomas. The malignant lymphoma, the reticulum cell sarcoma, the lymphoepithelioma, and the transitional cell carcinoma respond well to radiation but have a high recurrence rate. The epidermoid carcinoma is usually of a highly anaplastic variety and responds to radiation therapy but it also has a high recurrence rate. When the epidermoid carcinoma is of a mature cell type it exhibits considerable radio resistance. All of the lesions in this area are characterized by a marked tendency to metastasize. Metastases, while generally more resistant to the gamma ray than is the primary lesion, show remarkable regression under therapy. "The presence of cranial nerve paralysis is an unfavorable sign but does not necessarily make the case hopeless. Actual decalcification of the bones of the base of the skull is an almost certain fatal sign, but in all cases radiotherapy contributes a consider-

able amount of palliation and prolongation of life, even when the disease is not permanently controlled."[3] Disappearance of the primary lesion and its metastases under therapy is little cause for optimism. As has been stated the recurrence rate is high. Fifty per cent of the patients will develop recurrence, thirty-seven per cent within the first year. The recurrence is more resistant to therapy and the patient less able to tolerate adequate dosage.

The average life expectancy is determined by the symptoms and the cytological changes. Patients who exhibit ophthalmologic and neurologic symptoms run the shortest course, death occuring about fourteen months after the onset of therapy. The rapid clinical course of the well differentiated epidermoid carcinoma reduces the life expectancy of the carcinomas to about sixteen months. The sarcoma group survive about four to five months longer.

Despite the generally depressing picture five-year survivals have been reported in the larger series of cases. Various reports indicate twenty per cent of the patients surviving and free of symptoms. Godtfredsen reviewing the nine-year survival rate found a five per cent survival rate for the carcinoma group, and a twenty-five per cent rate for the sarcoma group. Godtfredsen's figures are based on the inclusion of the lymphoepithelioma and the transitional cell carcinoma among the mesodermal lesions related to the reticulum cell sarcoma. Those who classify these lesions as of epidermal origin would find an alteration in the percentage figures more favorable to the carcinoma group.

Careful routine examination of the nasopharynx may produce earlier diagnoses of malignancies in this area and consequently improve the poor prognosis that exists for patients with directing symptoms. When pressed for a prognosis as to cure and to life expectancy, we must be extremely guarded in our promises and place emphasis upon the fact that adequate therapy may produce the hoped for result. The prognosis depends upon the symptoms, the histology, the extention and metastases, and the experience and degree of cooperation between the radiotherapist and the otolaryngologist.

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XIII

THE RACIAL INCIDENCE (CHINESE) OF NASOPHARYNGEAL CANCER

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AND

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The racial susceptibility of Chinese people to cancer of the nasopharynx has been fairly well known for about the last twenty years.* Whether this predilection extends to other Oriental races is somewhat doubtful. Most of the clinical evidence relating to this phenomenon is contained in a number of reports from China and a few that have appeared from the United States and other Occidental countries. The present report deals with an over-all series of 358 cases of nasopharyngeal cancer observed and treated on the Head and Neck Service of the Memorial Hospital from 1935 to 1950. Among these cases there were 37 Chinese (10%). If, as we believe, there is acceptable statistical evidence that the Chinese, and possibly other Orientals, are more susceptible to nasopharyngeal cancer than

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*The predilection of minority groups to malignant growths in specific anatomic sites is of considerable interest in the study of the underlying nature of cancer. Examples of such predilections are illustrated by the following examples:

1. *Environmental or Climatic.*—The susceptibility of ourdoor workers subjected to sun and weather to cancer of the lower lip and exposed portions of the skin. The susceptibility of Egyptians to cancer of the urinary bladder supposedly due to nematode infestation.

2. *Occupational (usually chemical).*—Chimney sweeps' cancer of the scrotum from irritation of coal tar; cancer of the urinary bladder in aniline dye workers.

3. *Dietary.*—The predilection for mouth and gastrointestinal cancer in patients with nutritional (vitamin) deficiencies.

4. *Sex Endocrine.*—Cancer of the breast in females; mouth and larynx cancer in males; juvenile nasopharyngeal angiofibroma in pubescent and adolescent males—an apparently completely sex-linked tumor.

5. *Age.*—The general predilection of all forms of carcinoma for the older age groups.

Although none of the above-mentioned examples demonstrate the nature of the underlying cause of cancer, nevertheless, they may in the future cast considerable light on this subject by pointing to the associated conditions under which the underlying causative factors are most likely to produce cancer.

other races, then, so far as we know, this is the only example of racial susceptibility (excluding environmental factors) to a specific anatomic form of cancer so far established. A clear distinction should be made at this point between racial susceptibility independent of any environmental influence and a susceptibility due to some local or geographic environmental factor.

The Statistical Evidence of a Chinese Racial Susceptibility for Nasopharyngeal Cancer from a Review of the Literature.—As early as 1923, Thomson[13] had commented on the high incidence of what he termed "cervical lympho-sarcoma" among the Chinese living in and about Canton, China. Thomson mentioned in passing that 47 per cent of these patients complained of "nasal obstruction" which suggests to us that in these cases the primary lesion was actually in the nasopharynx—a contingency which was entirely missed by this author.

Other suggestive evidence is found in a report by Bonne[1] entitled, "Cancer and Human Races" in which the author comments on the peculiar frequency of malignant tumors of the cervical lymph nodes in Orientals. Bonne's data were obtained from autopsy records in some of the large medical centers of the Far East: namely, Batavia, Singapore, Manila, and Tokyo. He reported that from the anatomic standpoint malignant tumors of the lymph nodes of the neck ranked fifth in a large series of postmortem examinations among Malayans in Batavia, fifth among Chinese in Singapore, fourth in frequency among Chinese in Batavia, fourth among Filipinos in Manila, and none among the Japanese in Toyko. Bonne noted that *sometimes nasopharynx lesions were discovered late in the course of the disease, and he assumes that such invasion of the nasopharynx was secondary, that is, an extension from the primary site in the neck rather than the reverse.* (italics ours) This observer pointed out that the histologic appearance of the cervical lymph node masses resembled those commonly found primarily in nasopharyngeal cancer. In our opinion, Bonne's findings as regards the frequency of cervical lymph node cancer in Orientals can be reasonably interpreted as additional evidence of the high incidence of primary nasopharyngeal cancer in this racial group.

Since 1930, there have been several reliable reports from China regarding the relatively high incidence of nasopharyngeal cancer among the Chinese, and it is noteworthy that some of the largest series of this tumor have been reported from China, as for example, Digby et. al.[2, 3, 4] who recorded 103 cases in 1930 and an additional 114 cases in 1941. These were all patients from the surgical services of the Hong Kong University Hospital for the eight-year period

1930-1938. During this period, *cancer of the nasopharynx made up 18 per cent of all malignant tumors encountered in that institution.* In the Hong Kong University Hospital this anatomic site (nasopharynx) was exceeded in frequency only by cancer of the uterine cervix (28%); next in frequency after nasopharyngeal cancer came cancer of the breast (11%). Dunlap[6] cites another physician's experience who had observed 16 cases (5%) of nasopharyngeal cancer in a series of 336 tumor cases in a Changsha Clinic. These rates, 18 per cent and 5 per cent, far exceed the incidence of nasopharyngeal cancer in proportion to malignant tumors of all anatomic sites as observed at Memorial Hospital (1.1%) and in Macdonald's[8] survey of the Connecticut series (0.2%).* According to Digby, this high incidence of nasopharyngeal cancer is found not only in the region around Hong Kong and Canton, but also in such cities as Amoy, Swatow, Foochow, and Peiping.

Dunlap[6] reports from Shanghai that although non-Chinese patients constituted 60 per cent of his practice, all of his 16 patients with cancer of the nasopharynx were Chinese. The latest (1944) report from China is that of Wang[14] in which 36 cases are recorded from the Chengtu Eye, Ear, Nose, and Throat Hospital.

In the United States, Thompson and Grimes[12] (Philadelphia General Hospital) reported 2 Chinese (about 12%) in 17 cases of nasopharyngeal cancer; Lenz (New York) found 4 Chinese in 63 cases (about 6%). It is obvious that the racial makeup of the local population or, at least, of the patients applying for treatment may markedly influence the proportion of Chinese in any given series. New,[10] who in 1922 made a report of the first large series (79 cases) of nasopharyngeal cancer from the United States, did not mention any racial incidence, and it is fair to assume that the proportion of Chinese at the Mayo Clinic was not high. Simmons and Ariel[11] in a study of 150 cases of nasopharyngeal cancer from the Veterans Administration Hospital in Hines, Illinois, state that only one of their patients was Chinese. Martinez[9] in a report of 64 Chinese cancer patients observed in Cuba states that 20 (about 31%) had cancer of the nasopharynx.

Possible Explanations for the Susceptibility of Chinese to Nasopharyngeal Cancer.—If the Chinese and possibly other Orientals actually have a higher relative incidence of nasopharyngeal cancer than do other races, then there immediately arises the question of a reasonable explanation for this phenomenon. Dobson[5] in comment-

*The proportion of cancers in relatively inaccessible sites which are somewhat difficult, both in diagnosis and in treatment, can be expected to be higher in a cancer hospital than the proportion from general medical statistics.

ing on this racial susceptibility suggested as a causative factor the accumulated smoke from kerosene lamps, fireplaces, tobacco, and candles in the poorly ventilated Chinese houses. The validity of such a theory is impaired by the fact that nasopharyngeal cancer occurs also with unusual frequency in Chinese living under relatively better environments and frequently also in Chinese who have lived for many years or for practically all of their lives under an American standard of living. At Memorial Hospital we have observed several cases in Chinese professional men—physicians, merchants, and educators who had come to this country as children and had lived for many years under American standards of diet, hygiene, and sanitation. So far we have not observed a single case in an American-born Chinese. For the time being, at least, it seems safer to hold that the tendency is racial and/or inherited and that it is not determined by the immediate environment.

The Possibility of a Racial Susceptibility for Nasopharyngeal Cancer in Orientals Other than Chinese.—Since the Oriental races in general have at least a distant common origin, it would seem reasonable to suppose that groups other than pure Chinese would share in a susceptibility for nasopharyngeal cancer. The evidence here, though suggestive, is not definite. If Bonne's cases (of cervical lymph node cancer) can be assumed to contain at least a high proportion, or even a majority, of nasopharyngeal cancers, then it may be of significance that he mentioned a predilection among Malayans and Filipinos as well as Chinese. It is, nevertheless, curious that he found the tendency toward "cervical lymph node cancer" absent among the Japanese.

In this connection it may be of significance, as seen in Table 1, that at Memorial Hospital in a total of 52 cases of cancer in the upper respiratory and alimentary tracts in Orientals (Chinese, Filipino, Japanese, Korean, Indo-Chinese, etc.), there were 37 cases (71%) primary in the nasopharynx. The latter figure of 71 per cent is significant when compared to an expected incidence of only 5.5 per cent of nasopharyngeal cancer among the same regional sites in the over-all (Caucasian) population. Of equal significance is that all of our cases of nasopharyngeal cancer in the Oriental races were in Chinese. During this period we observed 7 cases of cancer of the mouth and pharynx in non-Chinese Orientals, but among these there were none which were primary in the nasopharynx.

Further Analysis of the Statistical Data from Memorial Hospital.—As has been previously mentioned, 37 cases of cancer of the nasopharynx in Chinese have been observed in the Head and Neck Clinic at Memorial Hospital in the fifteen year period 1935-1950. These 37 cases comprise about 82 per cent of all cancer of the head

TABLE 1.

INCIDENCE OF CANCER OF THE HEAD AND NECK IN ORIENTALS

As Observed in the Head and Neck Clinic, Memorial Hospital
During the Years 1935-1950

ANATOMIC SITES*	CHINESE		OTHER ORIENTALS
	CASES	PER CENT	NO. OF CASES
Buccal mucosa	0	..	1 (Filipino)
Floor of mouth	0	..	2 (Japanese)
Tongue	2	..	2 (Japanese)
Tonsil	1	..	1 (Indo-Chinese)
Thyroid	1	..	1 (Japanese)
Nasal Cavity	2	..	0
Nasopharynx	37	82%	0
Extrinsic larynx	1	..	0
Paranasal sinuses	1	..	0
TOTAL	45	100%	7

*Among Orientals admitted during this period there were no cases of cancer of such other anatomic sites in the head and neck as lip, gingiva, palate, pharyngeal wall, intrinsic larynx, and eye.

and neck in Chinese admitted to the Head and Neck Clinic of Memorial Hospital during the above-mentioned period. Among the 37 cases of nasopharyngeal cancer in Chinese there were three females (8%), as compared to 20 per cent females in nasopharyngeal cancer in Caucasians. This difference in sex incidence may be accounted for by the fact that the immigrant Chinese population in New York is preponderantly male.*

During this investigation several studies and calculations were made to determine the relative percentage of Chinese (as compared with Caucasians) admitted to the Memorial Hospital for cancer of

*According to the best sources available, the Chinese population of New York City may be estimated to be about 30,000. This figure includes the American-born Chinese and was obtained from the editorial offices of the "Chinese Journal." The Census Bureau has figures for 1940 only at the present time and reports a total of 10,370 (about 90% male) Chinese for New York County alone. Of these about 65 per cent were foreign born.

other head and neck sites and for cancer in general during the fifteen year period 1935-1949, inclusive. These may be briefly stated as follows:

During the years 1935-1949, inclusive, there were admitted to the Memorial Hospital Clinic about 7,100 Caucasians with cancer in various sites in the head and neck, exclusive of the skin and the major salivary glands. During the same period, 52 Orientals were admitted with cancer in corresponding anatomic sites; and of these, 45 were Chinese. Of the Chinese, 37 (82%) had cancer of the nasopharynx. The 37 cases of cancer of the nasopharynx was over four times the number of cases of cancers in other sites of the head and neck in Chinese, and two and one-half times the number of cancer of the head and neck in all Orientals.*

SUMMARY AND CONCLUSIONS

There appears to be a marked racial susceptibility (predilection) of Chinese to cancer of the nasopharynx. There is suggestive evidence that this susceptibility may be shared, at least to some extent, by all Oriental races, except the Japanese in whom there is, as yet, no statistical evidence of such a tendency. Such conclusions are based upon a survey of the literature and an analysis of the clinical and statistical data from the Memorial Hospital. In the Head and Neck Clinic at Memorial Hospital 45 cases in Chinese of cancer of the upper respiratory and alimentary tracts were observed during the fifteen year period 1935-1950. Of these, 37 (82%) were cancer of the nasopharynx as compared to an expected incidence of 5.5 per cent as based upon the over-all (mainly Caucasian) incidence in Memorial Hospital. As regards the incidence of cancer in Chinese and other Oriental races, the relative frequency in anatomic sites other than that of the nasopharynx appears to be the same as in Caucasians.

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*Those of the Staff of Memorial Hospital who are aware of the predilection of Chinese for nasopharyngeal cancer often utilize this knowledge by offering to wager, before any examination or interview, that an individual Chinese patient has cancer of the nasopharynx. The frequency with which such predictions prove to be correct always seem mysterious to the uninitiated.

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XIV

INTRAVENOUS PROCAINE FOLLOWING TONSILLECTOMY

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This investigation was initiated because of the many favorable reports in the literature of the efficacy of intravenous procaine in the relief of post-traumatic and post-operative pain and other distressing symptoms. No reference was found to the use of this agent for the relief of post-tonsillectomy pain.

It was believed if intravenous procaine proved to be beneficial for post-tonsillectomy pain it would have to be administered in a more concentrated solution and in a shorter period of time than the 1 liter of 0.1 per cent solution usually employed in other painful conditions. It was felt that few tonsillectomized patients, uncomfortable as most of them are, would choose to elect such a time-consuming procedure. Zeluff[4] emphasized this point in connection with treatment of other traumata, "Although in this country we are taught to avoid injecting 1 or 2 per cent procaine into a vein, the French inject 1 per cent procaine intravenously in doses of 100 to 200 mg (10 to 20 cc of a 1.0 per cent solution) over a period of 2 to 5 minutes for the same indications that we use solutions of 0.1 and 0.2 per cent. The possibilities of this method should be investigated, for if the drug can be given in this manner with reasonable safety, it would be advantageous from the standpoint of the amount of time saved and the promptness with which relief is obtained."

MODE OF ACTION

The exact mode of action of procaine is unknown. The results of some workers support the impression that the effect is central[5] but the relief of pain in traumatized or inflamed tissue is thought to be due mainly to peripheral action, the procaine crossing the permeable capillary membrane and bathing the terminal axone endings.[4] Musicant[6] has proven that procaine given intravenously will be con-

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centrated 7 to 8 times more in traumatized tissue than in normal tissue. The reason for the accumulation of the drug in the injured regions appears to be due to the increased capillary permeability.[3, 7, 8]

After accumulation in the tissues the onset of anesthesia depends on alkaline buffers present in the blood and tissue fluids setting free the anesthetic base from its acid attachment. The local anesthetic drugs are all esters of aromatic acids and are administered in the form of the salt of the common inorganic acids. The liberated base then dissolves in the lipoids of the nerve cells, which interferes with the transmission of sensory impulses from the cells.[9, 10]

It would appear, then, that an adequate concentration of the procaine in the traumatized tissues is the essential factor and it would seem reasonable to assume that this might be accomplished with a more concentrated solution even if injected in a shorter period of time than that usually employed with dilute solutions. Factors militating against the proper perfusion of the tissues with a more concentrated solution would be the lesser amount of fluid, the danger of toxic reaction, and perhaps a shorter time during which the procaine remains in the blood-stream. The latter point requires further elaboration.

Graubard, et al,[11] have shown that procaine injected intravenously disappears from the blood-stream almost completely in 10 minutes when given at the rate of 4 mg per kg of body weight in 20 minutes. Thus when 200 mg of procaine hydrochloride was injected intravenously into a 50 kg male only .004 mg per cc was detected in the blood in 10 minutes after injection and 500 mg injected intravenously into an 82 kg male produced only a trace in 10 minutes. The highest dosage used in this investigation was 400 mg in 2.0 per cent solution injected intravenously in 5 minutes. The usual rate of injection is 1000 cc of 0.1 per cent solution in 60 minutes and at this rate of injection it would take 24 minutes to introduce 400 mg, the largest amount used in this study. The dilute solution containing 400 mg of procaine would be in the blood stream, and thus perfusing the tissues, 24 minutes: the time required for the injection, plus the 10 minutes taken for the blood to clear itself of the drug. Assuming that it takes the blood stream the same amount of time to clear itself of the concentrated solution as of the dilute solution then the 400 mg in the concentrated solution would be perfusing the tissue 5 minutes, (the time for the injection) plus 10 minutes, (the time for the blood stream to clear itself).

The lethal dose of intravenous procaine for man is not definitely known but an estimate can be made by deduction from experiments on animals. Graubard, et al,[11] considered the tolerance of the rabbit

to procaine given intravenously to approximate closely that of the human. They found that 40 mg per kg of body weight injected rapidly into the rabbit caused immediate death. Shumaker[12] found the lethal dose of procaine injected rapidly into the veins of the guinea pig to be 41 mg per kg. Hatcher and Eggleston[13] found the lethal dose for the cat under the same conditions to be 40 mg per kg. From these experiments it is deduced that the dosages tolerated by these animals are about equal and that they are about the same as that for man. It should be emphasized, however, as stressed by Bieter[14] that a very considerable reduction below the minimal lethal doses for animals is absolutely essential when the drug is used clinically.

The safe dose, that is the maximum intravenous dose which can be injected rapidly without resulting in severe toxic reactions, is not exactly known. Deductions as to the probable safe dose, can also be made from the results of experiments on animals. Shumaker[12] using the guinea pig found the intravenous lethal dose to be one-tenth the subcutaneous lethal dose. It has been shown by the work of Allen, et al,[1, 2, 3] that the maximum safe dose, the central anesthetic dose, the convulsive dose and the fatal dose are all near the same end point. Allen[17] stated, "While retaining procaine for intravenous analgesia, we have abandoned it for general surgical anesthesia, because of the rare unpredictable collapse without convulsions and without known means of prevention." If we accept the premise that the safe intravenous dose is one-tenth the safe subcutaneous dose then we have a basis for estimating the safe intravenous dose as a result of recommendations resulting from extensive clinical use of the subcutaneous dose. Siegal[15] used 3000 mg subcutaneously and Labat[16] recommended as the safe subcutaneous dose 2,500 mg. From the above calculations it would appear that not over 250 to 300 mg of procaine can be safely tolerated in the blood stream at any one time. Based on an average 70 kg man this would be approximately 3.5 to 4.3 per kg of body weight.

The work of Hatcher and Eggleston and also that of Shumaker has shown that the concentration of the solution given intravenously makes little difference as to tolerance but that the limit is based directly on the rate of injection. In other words, the reaction of the animal is dependent on the concentration of the drug in the blood stream at any one time and no matter whether the solution being injected is weak or strong, as soon as a certain blood concentration is reached toxic symptoms or a fatal reaction will occur.

It was decided at the start of this investigation that only 1 per cent and 2 per cent solutions would be used. These strengths

are commonly used for local infiltrations and are generally readily available. A search of the literature revealed a number of reports of 1 per cent solution in various quantities being used but I was unable to find any report of the use of 2 per cent solution intravenously. Barber and Madden[18] have given 5 cc of a 2 per cent solution directly into the right ventricular cavity of the heart. This dose was given for cardiac arrest. The patient was also given cardiac massage and died 3 hours later with decerebrate convulsive seizures and Cheyene-Stokes respiration. The death could in no way be attributed to the use of the procaine. The highest dosage used in this investigation was 20 cc of 2.0 per cent solution injected in 5 minutes. This total of 400 mg would appear at first sight to be in excess of the theoretical safe dose of 250 to 300 mg as calculated above. If the 400 mg were injectd all at one time, say in 10 to 20 seconds, then the theoretical safe dose would definitely be exceeded. However, since Graubard has shown that the blood stream clears itself of procaine fairly rapidly, it was felt that at the end of the 5-minute injection period the blood stream would have already cleared itself of a fair amount of the procaine that was injected in the early part of the 5-minute injection. On the basis of milligram per kilogram per minute, the dosage used in this study does not exceed that which has actually been used both in man and experimental animals.

The solutions used were those made up in the hospital for subcutaneous use. These solutions are prepared in the hospital laboratory once weekly. The procaine hydrochloride is added to water triply distilled in a Barnstead still, equipped with a Spanish prison steam trap. The solutions are put up in rubber-capped 30 cc bottles and sterilized at 102° C. at 15 lbs. pressure for 15 minutes. The water is tested for pyrogens by the method described by Carter[19] and found to be free of contamination. Although Carter's test has been criticized as not being as delicate as the biological method of testing for pyrogens, it was thought for the purpose of this work it was of sufficient accuracy due to the small amount of solution used. The solutions are routinely made up and sterilized within 3 hours of the time of the distillation of the water.

Several workers have considered it necessary to prepare fresh solutions prior to each intravenous injection. I was unable to find any definite information as to why this practice was followed other than to be on the safe side in the event that any deterioration should take place in the solution. The breakdown products of procaine have been shown to be p-aminobenzoic acid and diethylaminoethanol, both of which are well tolerated by the body. Richards[20] has demonstrated that these split-products of procaine tend to ameliorate or

prevent procaine convulsions when the split-products are administered in high enough concentration. Richards stated, "The present observations lend support to the assumption that the two split-products of procaine attach themselves to the same receptors on which procaine acts. This competition may take place directly on the cells of the central nervous system or may occur on some intermediary enzyme component such as cholinesterase."

An estimate was made of the approximate age of the solution in the following way. An entire issue was newly made from the laboratory each week after it had been freshly prepared. The pharmacy drew its supplies from the laboratory once weekly and issued a complete stock once weekly from which the Eye, Ear, Nose and Throat Service drew its supplies. The Eye, Ear, Nose and Throat Service used up its stock of supplies about every two weeks. It was then probable that none of the procaine solution used was much over one month old.

METHOD OF EXAMINATION

It was felt that the best criteria of the usefulness of the drug would be the relief of the pain as experienced and reported by the patient. It was also appreciated that the manner in which the purpose of the medication was presented to the patient would perhaps in some instances psychologically influence his estimate of the efficacy of the medication. The patients were routinely told that an injection was to be given to help heal the raw areas in the throat, but no mention was made at that time that the drug was being evaluated as an analgesic agent. It was believed that the majority of the patients, because of the necessary measurements taken in conjunction with the injection of the drug, would realize that some sort of an investigation was being made. It was thought that a more objective answer would be obtained if the patient was not appraised of the true nature of the investigation during the test period. The nature and extent of the analgesic effect were determined by questioning during routine examination the following day. Two simple clinical tests, to some extent objective, were used to determine whether the pain had been diminished as a result of the injection. A previous series of 15 patients who had had a tonsillectomy the day before were sprayed in one tonsillar fossa with 0.1 per cent pontocaine solution. After a 3-minute wait in order to give the pontocaine time to take effect, each fossa was then probed with an applicator. It was found without exception if the patient had not used other medication recently that there was a pain threshold differential between the two fossae after one side had been sprayed with the pontocaine solution. The sprayed side was always the less painful to probing. It was decided

to use this test as one of the criteria for the abolition of pain, for if the procaine abolished the pain threshold differential between the two sides after one side had been sprayed with 0.1 per cent pontocaine, it would establish that the procaine intravenously was equal to or better than the pontocaine spray in diminishing the pain in the fossae.

The other partially objective test used was to measure the bite before and after the procaine injection. The patient at the time of the first measurement was told to open his mouth to the point where he first experienced some pain and then to hold his jaw still in this position. A reading was then taken with a millimeter rule between the occlusal surfaces of the upper and lower incisor teeth. After the procaine injection the patient was told to open his mouth again to the point where he felt about the same amount of pain as at the time of the first determination, and the measurement was again taken.

Since in the first 18 patients who were given the lowest dosage, it was found that with but few exceptions an analgesic effect was being exerted as determined by the objective tests, it was decided to discontinue these measurements for the higher dosages of the drug. With these measurements eliminated the injections would have more of the appearance of a routine medication and would not be so apt to arouse the resentment or enthusiasm of the patient because of being included in an experimental study.

The tonsillectomies were done in the afternoons and the injections of procaine were given the following morning. The routine premedication for tonsillectomy was 3 grains of pentobarbital sodium by mouth; 1/6 grain of morphine sulfate and 1/100 grain of atropine sulfate, both by hypodermic injection; all premedication to be given approximately 1 hour prior to operation. Standing orders on the ward were that the patient could have 1½ grains of pentobarbital sodium for sleep if needed, one grain of codeine sulfate by mouth for pain if needed, and acetylsalycilic acid could be had at any time. No patient was to receive any medication from the nurse on the ward on the morning following the operation until after the patient was seen in the clinic. After the patient had been seen in the clinic and the procaine injection made, he was to be allowed to have acetylsalycilic acid if he asked for it. Although it is believed that these orders were generally carried out, some of the patients were discovered to have brought Aspergum to the hospital and to have chewed some on the morning prior to the tests. None of the patients, other than those designated in the tables as having chewed Aspergum, admitted having any medication on the morning prior to the procaine injection.

Six of the hospital internes assisted with this investigation. As the patient reported to the clinic in the morning, the interne would look at the throat, take the bite measurement, spray one of the fossae with 0.1 per cent pontocaine and in 3 minutes test the sensitivity of the two fossae. The patient was then told he was to be given an injection to help heal his throat and was taken to another room and placed recumbent on an examining table where the blood pressure and pulse rate was taken. I then gave the patient the injection of procaine. After the injection the interne again took the blood pressure and pulse rate. The patient was allowed to lie on the table for about 5 minutes following the injection and was then taken to an examining chair where the same interne again took the bite and determined the sensitivity of each fossa. As mentioned previously, the bite and pain sensitivity of the fossae were not continued after the first series of patients was completed. Patients given the higher dosages were weighed just prior to giving the procaine injection.

Pentobarbital sodium was kept at hand to be given intravenously in case convulsions should occur, and epinephrine was also ready in the event of respiratory depression. It was never necessary to use either of these drugs. No procaine sensitivity tests were performed prior to injection as all patients had had tonsillectomy under procaine-epinephrine local anesthesia the day prior to the test.

INTERPRETATION OF RESULTS

The first series of cases totaled 18 in number. The patients were given 10 cc. of 1.0 per cent procaine hydrochloride intravenously in 5 minutes. Four of these 18 patients demonstrated no difference in the pain threshold of the two tonsillar fossae after one fossa had been sprayed with 0.1 per cent pontocaine solution. Three of these patients admitted having chewed Aspergum just prior to being tested. Of the 14 remaining patients who had a pain threshold differential after one fossa was sprayed with the pontocaine solution, all showed obliteration of this pain threshold differential between the two fossae after they had received the intravenous injection of procaine. All but 5 of the 18 patients had a wider bite after the procaine injection than before and one of the 5 patients admitted chewing Aspergum prior to the test.

The relief of pain in these 18 patients varied from 0 to 6 hours with an average duration of approximately 2 hours. The blood pressure or pulse rate was not perceptibly altered in this group and subjective symptoms during injection were minimal.

Many of the patients in the 3 different groups had some dilatation of the pupils, perspiration of the head and neck, and other symptoms and signs which have been described by other authors, particularly by Allen and Graubard and his associates.

The second series of cases totaled 20 in number. The patients were given 10 cc of 2 per cent procaine intravenously in 5 minutes. There were 4 patients who reported no noticeable analgesia following the injection, and none of these admitted having medication prior to the test. The analgesia for all patients ranged from 0 to 10 hours with an average of just a little under 4 hours time. The subjective symptoms during injection were somewhat more marked as a general rule than in the group which received the lower dosage.

There were only 3 patients in group 3 who received 20 cc of 2 per cent novocaine intravenously in 5 minutes. In each of the 3 patients central anesthesia was beginning to take effect as evidenced by two being unable to talk and one being irrational for several minutes. It was obvious that the dosage was too high for routine post-tonsillectomy use so that no further injections of this strength and amount were given. The analgesia in this group averaged between 9 and 10 hours.

In none of the three series of patients were any severe reactions encountered. No patient required any medication to countract any symptoms resulting from the injection. All patients either walked back to the ward, or were discharged from the hospital, within a few minutes following the injection. There was no muscular twitching seen which is reported by several authors to be the immediate forerunner of convulsions if the procaine is pushed further.

The results show a higher procaine level at the 15-minute period than was originally anticipated, and the level is considerably higher at the 10 minute interval than was found by Graubard[11] when he injected 4 mg per kg of body weight in 20 minutes. These tests were determined by the technic described by Ting, et al.[21]

DISCUSSION

This investigation could be criticized on purely scientific grounds for several reasons; there was no rigid control maintained on the use of other analgesic drugs, the same objective tests were not carried out on all series of patients, the third series of cases was too small in number, the blood procaine levels were not carried out over a long enough period of time, and all symptoms and signs during injection of the drug were not recorded in detail. The purpose of this investigation was not to make a detailed study of the pharmacological properties of the drug in the dosages given.

The investigation was undertaken to determine if procaine could be given intravenously in concentrated dosages as a useful clinical therapeutic agent for post-tonsillectomy pain under average hospital conditions. It was intended that if the results of this initial survey appeared to be promising, then a further series of cases would be investigated in which additional data would be obtained, such as the optimum therapeutic dose, the tissue concentration of the drug in the traumatized area (tonsillar fossa) and in a nontraumatized area (floor of mouth), more detailed objective pain threshold tests to determine how long the analgesic effect of the drug lasted, and more prolonged blood procaine level determinations to find the time when the procaine was completely cleared from the blood stream.

In this survey a group of patients was tested under the conditions stated until it was felt a reasonable conclusion could be drawn from the clinical results of the particular test. The conditions were then changed to determine additional information. The patients were taken as they appeared on the operation schedule, and no patient was particularly chosen or eliminated from the test for any reason.

CONCLUSION

It was concluded from this study that a concentrated solution of procaine given intravenously is not a useful therapeutic agent for post-tonsillectomy pain. It is significant that not a single patient in this study requested another injection of the drug at any time following his initial injection. The reason for this uniform lack of enthusiasm for the medication was not because it failed as an analgesic agent but because of the unpleasant symptoms experienced by the patient during the injection of the drug.

SUMMARY

1. Good results have been reported with a dilute solution of procaine given intravenously for a variety of traumatic and painful conditions.

2. A discussion is made concerning the probable safe therapeutic intravenous dosage of procaine.

3. Forty-one patients were given intravenous procaine injections the day following tonsillectomy, 18 were given 10 cc of 1.0 per cent, 20 were given 10 cc of 2.0 per cent, and 3 were given 20 cc of 2.0 per cent, all injections being given in a 5-minute period.

4. The patients given 10 cc of 1.0 per cent solution experienced analgesia of the tonsillar fossae lasting for an average of 2 hours;

those given 10 cc of 2.0 per cent about 4 hours, and those given 20 cc of 2.0 per cent about 9½ hours.

5. It was concluded that the unpleasant symptoms experienced by the patient during injection of the procaine precluded the usefulness of the drug as a routine post-tonsillectomy analgesic agent.

6. Blood-procaine levels were determined on four patients injected intravenously with 10 cc of 2.0 per cent procaine and one patient injected with 20 cc of 2.0 per cent procaine, the levels being determined at 1, 5, 10, and 15-minute intervals following the intravenous injection. It was found that a fairly high level of procaine remained in the blood stream of all of these patients 15 minutes following the intravenous injection.

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Fitzsimons Army Hospital.

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XV

NYSTAGMUS RELATED TO LESIONS OF THE CENTRAL VESTIBULAR APPARATUS AND THE CEREBELLUM

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The relative frequency of dizziness and an accompanying nystagmus in patients seen by the otolaryngologist and the neurologist, and the probable importance of the direction of nystagmus for localizing the lesion and for the proper clinical diagnosis, prompted the present study. The comprehensiveness of the subject of nystagmus necessitates limiting the scope of this investigation to the relatively less well known role of the individual vestibular nuclei and to the regulatory effect of the cerebellum over these nuclei.

The vestibular nuclei, located in the cephalic end of the medulla and the caudal part of the pons, are four in number (Fig. 1: M,L,S,I.): the medial or principle nucleus, the superior or von Bechterew's nucleus, and the connecting inferior and lateral vestibular nuclei. All these nuclei and the cerebellum receive fibers from the bipolar cells of the vestibular ganglion (Fig. 1:VG) lying in the internal auditory meatus. From the lateral and medial vestibular nuclei there are crossed and uncrossed fibers through the medial longitudinal fasciculus to the abducens nucleus (Fig. 1:VI N.N.). From the superior vestibular nucleus, fibers pass in the homolateral medial longitudinal fasciculus (Fig. 1:MLF) to the motor nuclei of the trochlear and the oculomotor nerves.[1]

The usually diagramed connections indicate that a single vestibular nucleus may be connected directly, without synapse, with all the contralateral (and in some cases with the homolateral) eye muscle nuclei. Stimulation of such a pathway should cause rotary or irregular eye movement rather than the observed orderly conjugate deviation. The fibers crossing the midline from the lateral vestibular nucleus, accompanied by those from the medial vestibular nucleus, bifurcate in the medial longitudinal fasciculus with rostral connections with

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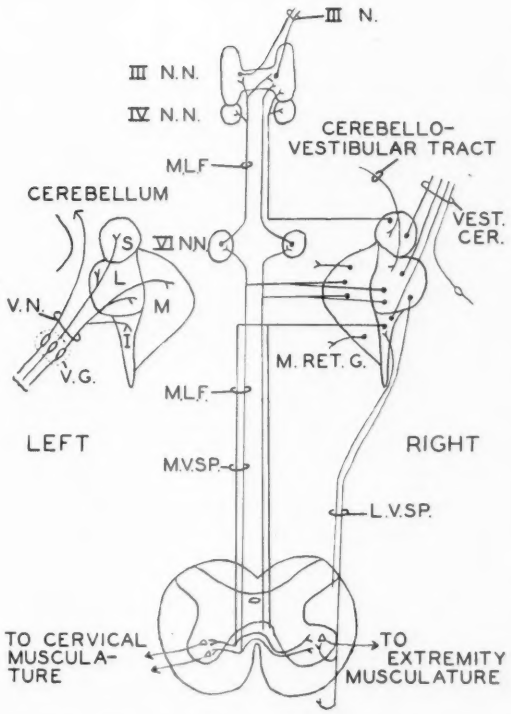

Fig. 1.—*V.G.*, Vestibular Ganglion; *V.N.*, Vestibular Nerve; *S*, Superior; *L*, Lateral; *M*, Medial; *I*, Inferior; *V.N.*, Vestibular Nuclei; *M.L.F.*, Medial Longitudinal Fasciculus; *M.V.S.P.*, Medial Vestibulo-Spinal Tract; *L.V.S.P.*, Lateral Vestibulo-Spinal Tract; *M.RET.G.*, Medial Reticular Gray; *VI N.N.*, Abducens Nucleus; *IV N.N.*, Trochlear Nucleus; *III N.N.*, Oculomotor Nucleus; *III N.*, Oculomotor Nerve; *VEST. CER.*, Vestibulo-Cerebellar Tract.

the abducens nucleus, as described, and caudal connections by crossed and uncrossed fibers of the medial vestibulo-spinal tract, to motor nuclei supplying cervical masculature (Fig. 1). From the lateral vestibular nucleus a group of directly descending uncrossed fibers forms the lateral vestibulo-spinal tract (Rasmussen[2]). These fibers synapse with ventral horn cells throughout most of the spinal cord, mainly with those which innervate the musculature of the extremities (Fig. 1). These connections are of importance, of course, in righting reflexes.[3]

The medial vestibular nucleus sends short internuclear fibers to the medial reticular gray and to the dorsal efferent nuclei of the

vagus nerves. These latter connections are of importance in motion sickness and vomiting.

From the vestibular nuclei impulses pass to the cerebellum (Fig. 1: Vest. Cer.). There are efferent cerebellar fasciculi from the cerebellar nucleus tecti, or fastigius, which, after partial decussation, cross the midline in the roof of the fourth ventricle and then pass through the inferior cerebellar peduncle to the lateral vestibular nucleus. Through impulses passing over this cerebello-vestibular system, the cerebellum exerts a regulatory effect over this vestibular area. The nucleus fastigius is, in turn, under the regulatory or inhibitory action of the ipsilateral pyramis of the cerebellar cortex, which receives impulses from the contralateral cerebral cortex by way of the cortico-ponto-cerebellar system with synapse in the pontine gray[3, 4, 5, 6, 7] (Fig. 3).

In the following experiments, the vestibular area of Macaca mulatta was entered with an insulated electrode through a trephine opening in the skull. The monkey and the needle were held immobile by a calibrated stereotaxic instrument, the McCullock modification of the Horsley-Clarke apparatus. Mathematical determination of the depth and direction of penetration of the needle tip was made by reference to the excellent charts of D. Atlas and W. R. Ingram (1937).[8]

The right lateral vestibular nucleus was entered first and stimulated with a low faradic current. This produced a slow conjugate movement of the eyes to the left, or a nystagmus with rapid component to the right. The impulses set up in the right lateral vestibular nucleus were carried across the midline to the medial longitudinal fasciculus and abducens nucleus of the left side, stimulation of the left abducens nucleus causing contraction of the left lateral rectus muscle. Secondary fibers from the parabducens portion of the abducens nucleus passed to that portion of the oculomotor nucleus known as the nucleus of Perlia, where they synapsed with cells sending fibers in the oculomotor nerve to the right medial rectus (Fig. 2). Simultaneous contractions of the left lateral rectus and the right medial rectus produced a conjugate deviation of the eyes to the left.

From the right vestibular nucleus fibers also ascend in the medial longitudinal fasciculus of the same side to the abducens nucleus (Fig. 2: dotted line). Such fibers carry impulses which inhibit the discharge of the abducens nucleus to the homolateral lateral rectus muscle; consequently, the lateral rectus of the right side is relaxed when that of the left side contracts. There is a similar relation established between the two medial recti.

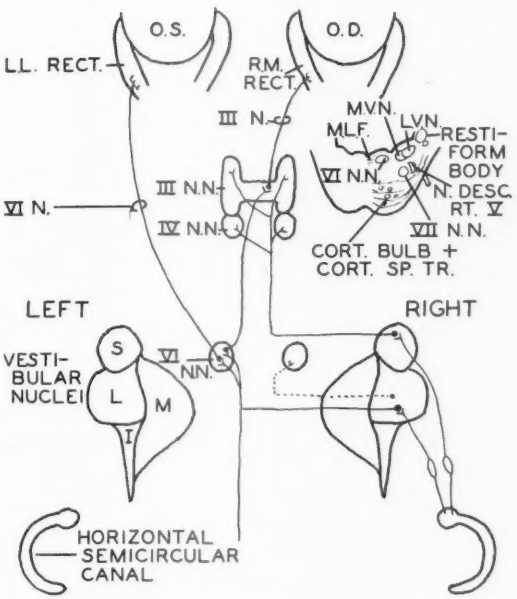

Fig. 2.—*L.L. RECT.*, Left Lateral Rectus; *O.S.*, Left Eye; *R.M. RECT.*, Right Medial Rectus; *O.D.*, Right Eye; *III N.*, Oculomotor Nucleus; *IV N.N.*, Trochlear Nuclesu; *VI N.N.*, Abducens Nuclesu; *VI N.*, Abducens Nerve.

Key Diagram: Section of lower pons through the lateral and medial vestibular nuclei *M.V.N.*, Medial Vestibular Nucleus; *L.V.N.*, Lateral Vestibular Nucleus; *M.L.F.*, Medial Longitudinal Fasciculus; *N. DESC. RT. V*, Nucleus of the Descending Root of V; *VII N.N.*, Facial Motor Nucleus; *CORT. BULB.* & *CORT. SP.*, Cortico-Bulbar and Cortico-Spinal Tracts.

If, as stated by Spiegel, the origin of both components of nystagmus is in the vestibular nuclei, the resulting right nystagmus (rapid component) may be viewed as due to stimulation of fibers from the vestibular area through the homolateral medial longitudinal fasciculus to the abducens nucleus of the same side. Lorente de Nó[9] believed the origin of the quick component to be in the adjoining reticular substance.

Repetition of these experiments on other monkeys produced the same results. These results parallel an irritative lesion of the peripheral labyrinth; or a reflex left movement of the eyes on turning to the right; or the nystagmus produced by rotating a patient to the left, stopping the chair and observing the nystagmus towards the stimulated right ear.

It was found that depth of anesthesia influenced the results. Too deep an anesthesia could abolish both components of nystagmus; too light an anesthesia roduced a variety of eye movements, probably of cerebral origin. After stimulation, a nystagmus, opposite in direction to that obtained during stimulation, was occasionally noted. It was felt to be due to fatigue with consequent lowering of the functional activity of the cells on the stimulated side, and a resulting imbalance between the vestibular areas of the two sides.

The right lateral vestibular nucleus was then destroyed by use of a coagulating current with replacement of the needle to produce contiguous one-millimeter areas of necrosis. This caused a horizontal nystagms with a rapid component to the left. This reversal should be expected because of the imbalance thus set up between the vestibular nuclei of the two sides. The left side exerted relatively greater effect, and produced the nystagmus to its side, such a result is in accordance with the Sherrington-Hering law of reciprocal inhibition of antagonists, as applied to the vestibular nuclei by Bartels and De Kleyn. The resulting nystagmus parallels a destructive end organ lesion as in suppurative labyrinthitis, with nystagmus to the opposite side. On recovery from anesthesia this monkey showed marked ataxia with a tendency to fall to the right from interruption of the outer part of the right inferior cerebellar peduncle, also. The monkey stood and sat with a wide base and could be more easily rolled to the right than the left. There was marked hypotonicity of the right arm and leg. The head tilted to the right.

Rotation of this animal to the right did not produce the normal left deviation of the eyes. However, left rotation caused normal right deviation. There was no post-rotational nystagmus on rotation to the left. Right rotation produced normal left post-rotational nystagmus.

After allowing two weeks' time for degeneration of nerve tracts, the monkey was perfused with formalin and the brain sectioned and stained. The Marchi preparation revealed degeneration of fibers from the destroyed lateral vestibular nucleus. These fibers crossed the midline in the medial longitudinal fasciculus and ended at the abducens nucleus. No degenerated fibers were found in the medial longitudinal fasciculus above the abducens nucleus. These facts furnished the basis for our diagram showing a synapse in the abducens nucleus. If the impulse from the lateral vestibular nucleus had passed to all the eye muscle nuclei of the opposite side, as usually diagramed, a pure horizontal nystagmus would not be possible.

Similar experiments, carried out on other monkeys, brought out more clearly that if a slight stimulus produces a nystagmus, a too

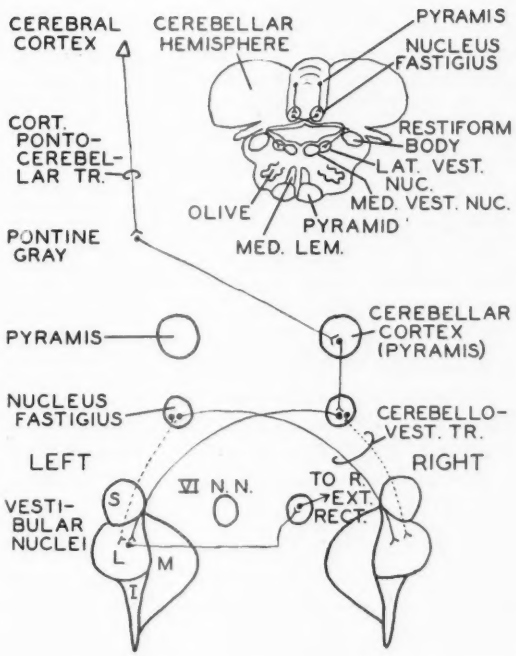

Fig. 3.—*CORT.-PONTO-CEREBELLAR TR.*, Cortico-Ponto-Cerebellar Tract; *VI N.N.*, Abducens Nucleus; *TO R. EXT. RECT.*, To Right External Rectus Muscle; *CEREBELLO-VEST. TR.*, Cerebello-Vestibular Tract.

Key Diagram: Section through upper medulla and cerebellum to show medial and lateral vestibular nuclei, pyramis, and nucleus fastigius. *LAT. VEST. NUC.*, Lateral Vestibular Nucleus; *MED. VEST. NUC.*, Medial Vestibular Nucleus; *MED. LEM.*, Medial Lemniscus.

great stimulus may reduce the nystagmus by causing a certain amount of destruction and, with still greater destruction, there is a reversal of the nystagmus and conjugate deviation toward the side of the lesion. Moreover, small destructive lesions with their peripheral area of irritated cells, were occasionally seen to produce the effect of stimulation.

In another experiment the right lateral vestibular nucleus was again stimulated with a resultant right horizontal nystagmus (i.e., the quick component to the right). A destructive lesion was made here. The needle was advanced at one millimeter intervals toward the superior vestibular nucleus and the nystagmus showed a progressive change from left horizontal to left oblique (mainly horizontal),

to left oblique (mainly vertical), to a pure vertical nystagmus. This agreed with the findings of Marberg, Teidler, and Stengel. A destructive lesion was then made in the right superior nucleus. On recovery from anesthesia the monkey crawled in a circular movement to the left, occasionally falling and rolling over to the right. At a later date this monkey was given a light anesthesia and a left oblique and a left horizontal nystagmus were observed. This was felt to be due to an imbalance between the nuclei of the two sides, the intact left side producing the nystagmus as had been previously observed. To confirm this supposition the intact right medial vestibular nucleus was stimulated and was found to inhibit repeatedly the spontaneous nystagmus produced by the left side. In addition to inhibition of the spontaneous right nystagmus there was produced, during stimulation, a steady conjugate deviation of the eyes to the left, thought to be due to action of the right medial nucleus with the rapid component suppressed by destruction of the right lateral nucleus. At this point a destructive lesion was made in the right medial nucleus. This accentuated the existing left horizontal and oblique nystagmus. Thus it was felt that the lateral and medial nuclei of the same side coordinated in action in producing the rhythmic eye movement, with the quick component in the same direction.

A clinical example of these experimental findings is given by the following case:

G. S. a 52 year old white insurance salesman, receiving treatment for diabetes mellitus and chronic suppurative left frontal sinusitis with a draining fistula and osteomyelitis of the frontal bone, developed vertigo and falling to the left, hoarseness, numbness of the left side of the face and some diplopia. In addition to the findings related to his sinusitis, the examination revealed a loss of appreciation of temperature and pain over the left half of the face and right half of the body. Motor examination for coordination showed impaired finger to nose and heel to knee to toe tests on the left. Further examination revealed falling to the left, right horizontal and vertical nystagmus, impaired external ocular movements on the left, left ptosis and miosis producing a Horner's syndrome and left palatal pharyngeal and laryngeal paralysis. The neurological consultant concurred in the diagnosis of a posterior inferior cerebellar artery thrombosis and felt that one might hypothesize a high distribution of the artery.

This case demonstrates a destructive lesion of the left vestibular nuclei with the right nystagmus produced by the intact right vestibular nuclear area. Falling in the direction of the slow component of the nystagmus here might indicate interference with the inferior cerebellar peduncle.

In another experiment, the right side of the pyramis of the cerebellum was stimulated using the suboccipital approach, with a resultant slow right conjugate deviation of the eyes. This was interpreted as showing the regulatory or inhibitory effect of the pyramis over the

nucleus fastigius of the same side, and the inhibitory effect, in turn, of the nucleus fastigius over the lateral vestibular nucleus of the opposite side (Fig. 3). Thus the stimulation of the right pyramis released the left vestibular nucleus from the inhibiting action of the right nucleus fastigius and causes a right deviation of the eyes (left nystagmus). Stimulation of the left pyramis caused left deviation of the eyes. Impulses over the uncrossed fibers from nucleus fastigius to the vestibular nuclei (Fig. 3, dotted lines) were felt have an opposite effect to those over the crossed fibers; that is, an effect comparable to that of the previously discussed uncrossed fibers from the lateral vestibular nucleus to the abducens nucleus (Fig. 2).

Destruction of the region of the right pyramis was next tried and, as expected, a reversal with right nystagmus was found. In effect, this destruction released the right nucleus fastigius from the inhibitory action of the cerebellar cortex so that it could exert its maximum inhibitory effect over the left vestibular area. With the resulting imbalance, the right lateral vestibular nucleus was dominant and produced its characteristic nystagmus to its own side.

To further confirm this double system of inhibition, the right nucleus fastigius was stimulated and a slow conjugate eye movement to the left noted (right nystagmus). The result of this stimulation presumably caused greater inhibition of the left vestibular nucleus and allowed the less inhibited right lateral vestibular nucleus to discharge.

The following two cases will illustrate the use to which these findings may be put:

I. W. a 38 year old farmer, was admitted to the hospital with the history of a draining left ear for 20 years. Drainage had been constant for 18 years. Three weeks prior to admission he noted frontal and occipital headache, nausea, and vomiting. On the day of admission, diplopia and nystagmus began.

On examination the right ear was normal. The left ear revealed a scant amount of non-odorous exudate in the canal. The drum was markedly thickened and scarred. There were three perforations: an antero-inferior and a posterior attic perforation, each with a tiny polyp, and a small posterior central perforation. There was no mastoid tenderness. On testing the hearing there was no response on the left to a shouted voice with the right ear masked with the Barany noise box. A marked coarse first degree nystagmus to the left was present on left gaze, and the patient was definitely able to turn his eyes easier to the right than to the left. No papilledema was present. There was past pointing and falling to the right, equivocal adiadokokinesis of the left hand, and poor performance of the finger to nose and heel to knee to toe test on the left. Slight nuchal rigidity and photophobia were observed. Mastoid x-rays revealed a sclerotic mastoid with extensive destruction in the antral and retrofacial regions. Routine blood count showed 15,300 white cells, with 88 per cent polymorphonuclear leucocyates. Spinal fluid revealed a pressure of 95 to 100 millimeters of water, 270 cells with 65 per cent polymorphonuclear leucocytes, 35 per cent lymphocytes, Pandy +, and normal sugar.

On the day following admission a left radical mastoidectomy was done and the mastoid found to be extensively excavated by a cholesteatoma in the antral and retro-facial regions. In the latter the bony defect extended deeply medial to the sigmoid sinus. There was a round exposure (1.5 cm in diameter) of the cerebellar dura, covered by a cholesteatomatous matrix with a slightly reddened and roughened surface. The lateral canal was well delineated but intact. The patient was followed closely after operation; he was seen to be very lethargic in the afternoons although he was mentally clear in the mornings. On his second postoperative day, the neurosurgeon noted that bilateral Babinski signs were present. Pulse and blood pressure were within normal limits. A suboccipital trephine, midway between the left mastoid and the midline, was done. When an exploring needle was inserted for four centimeters an abscess cavity, with no definite capsule but containing 5 cc of thick yellow-green pus, was encountered. Following the drainage of the abscess the patient made an uneventful recovery. Three weeks postoperatively he felt shaky but was increasingly steady on his feet, although he was still somewhat ataxic, staggering in either direction. The nystagmus had disappeared.

This interesting case put to test our experimental findings. The differential diagnosis was, of course, suppurative labyrinthitis with an early irritative stage of meningeal invasion. This diagnosis was supported by the results of the hearing test and by the nuchal rigidity. However, on the basis of experimental evidence, the nystagmus toward the diseased ear could be explained only by a serous labyrinthitis with irritative, rarely observed, nystagmus to its side or by a destruction of left cerebellar cortex or white matter. Such cerebellar destruction would release the left nucleus fastigius from the inhibitory action of the cerebellar cortex and increase its inhibitory effect upon the right lateral vestibular nucleus. Thus an imbalance would be set up between the lateral vestibular nuclei of the two sides. The discharge from the uninhibited left vestibular nucleus would tend to produce a right conjugate deviation of the eyes, with difficulty in turning the eyes to the left and a left nystagmus on attempting to do so. The diagnosis of cerebellar involvement was favored before the clinical course proved it to be correct.

E. L., a 7 year old negro boy, entered the hospital with a three months' history of headache and occasional vomiting. In the past month the headaches had been increasing in severity and diplopia was noticed. For three weeks prior to admission the patient had an ataxic gait.

The general physical examination was negative. The neurological examination revealed a horizontal nystagmus in the direction of lateral gaze, predominately to the right. Upper gaze was normal. Two to three diopters of papilledema were present bilaterally. The upper extremity reflexes were hypoactive and equal. The right knee jerk was hypoactive. The Babinski and Hoffman reflexes were not present. The muscular tone was good, and no atrophy or weakness was present. Sensation was normal. The patient was unstable, standing with a wide base, and showed a tendency to stagger to the right. The cerebellar tests showed bilateral ataxia, worse on the left, on performing the finger-to-nose and heel-to-heel-to-toe tests. Rapid movements were poorly performed on the left. No rebound was present.

X-ray examination of the skull revealed widening of the coronal sutures with a slight osteoporosis and a sharpening of the posterior clinoid processes character-

istic of increased intracranial pressure. The ventriculogram showed an internal hydrocephalus involving the entire ventricular system down to the region of the fourth ventricle. The fourth ventricle and the aqueduct of Sylvius were not visualized on lateral views but on sagittal views, with the brow down, there was air in the fourth ventricle and aqueduct. The fourth ventricle was indented on the right and displaced to the left by a space-occupying lesion in the region of the right cerebellar hemisphere.

At operation a large midline tumor, with extension to the right, was found in the fourth ventricle. The tumor occupied a considerable part of the vermis and rested on the floor of the fourth ventricle. A large amount of tumor was removed, exposing the cerebral aqueduct and establishing free communication.

Later, respiratory distress from subglottic edema from the intratracheal tube necessitated tracheotomy. At this time there was nystagmus in the direction of lateral gaze but now predominantly to the left.

This case demonstrated a cerebellar lesion with a predominant nystagmus to the side of the lesion, preoperatively. The direction of the nystagmus changed after operation. The neurosurgeon believed, that, in exposing the aqueduct some of the under part of the vermis of the cerebellum was injured and, probably, the right nucleus fastigius was destroyed. Such destruction would reverse the nystagmus.

SUMMARY

1. Stimulation and small irritative lesions of the lateral and medial nuclei produce horizontal nystagmus to the same side.

2. Larger lesions, causing destruction of tissue, produce nystagmus to the opposite side, and falling and tilting of the head to the same side.

3. The direction of the nystagmus is influenced not only by the magnitude of the stimulus and the extent of destruction, but also by the depth of anesthesia and by fatigue phenomena (after stimulation reversal of nystagmus).

4. Lesions of the superior vestibular nucleus cause vertical nystagmus; oblique nystagmus results from lesions at the transition between the superior and lateral vestibular nucleus.

5. Destructive cerebellar lesions, particularly in the region of the pyramis, cause nystagmus to the same side (deviation to the opposite side). Apparently this is true whether the lesion involves the cerebellar cortex or the central white matter. However, if the lesion extends deeply enough to involve the nucleus fastigius, a reversal of the nystagmus to the opposite side is to be expected.

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XVI

EXTRADURAL HEMORRHAGE AS A COMPLICATION OF OTOLOGICAL AND RHINOLOGICAL INFECTIONS

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Massive extradural hemorrhage due to erosion of blood vessels by otological or rhinological infections is an extremely rare complication. A check of the classical text books and a review of the literature on extradural hemorrhage and infections of the ear, nose, sinuses, and skull have failed to reveal any reference to this entity. We wish to report in this paper two cases in which the lesion was found. In the first instance an extradural hemorrhage occurred in the middle fossa following the erosion of a large vessel by a chronic middle ear infection. In the second case a similar lesion was found in the anterior fossa following furunculosis of the nose with secondary osteomyelitis of the frontal bone. These two cases are presented in the hope that our experience may aid in the early diagnosis and treatment of similar lesions.

Case 1.—J. Y., 21 years, white male, admitted to the Otology Service at University Hospital, Ann Arbor, on the evening of January 15, 1948 with a history of chronic recurrent middle ear infection secondary to trauma fifteen years before. A few weeks prior to admission he developed a draining right ear with right temporoparietal headache, nausea, and vomiting. For twenty-four hours previous to admission he had been moderately drowsy. His physician had given him three injections of penicillin intramuscularly daily for five days. On close questioning the patient gave no history of head injury except for the trauma fifteen years previously.

Upon neurosurgical consultation 6 hours after admission, the following picture was present. The blood pressure was 140/80, the pulse 82, the respirations 22. The patient was lethargic, but could be readily roused and gave accurate responses to the examiner's questions. There was a slightly bloodtinged discharge from the right

ear. The right pupil was more dilated than the left, but both reacted to light. The discs showed some peripheral blurring, but vessels could be visualized well down into the optic cup. No hemorrhages or exudates were observed in the fundi. The cranial nerves were normal. There was equivocal weakness of the left upper extremity, but the remaining extremities exhibited normal strength. The sensory examination and status of co-ordination could not be accurately evaluated. Deep reflexes were equal and active. Babinski and Chaddock signs were positive bilaterally.

Skull x-rays appeared normal. The pineal gland was not calcified, and there was no abnormal intracranial calcification. A diagnosis was made of probable right temporal lobe abscess.

Examination was concluded at one o'clock in the morning, at which time the patient's vital signs were normal. Since the patient had no papilledema and was able to converse intelligently when aroused, ventriculography was deferred until eight o'clock that morning, at which time it was felt that more satisfactory x-rays could be obtained. The head was completely shaved; the blood pressure, pulse, respirations and the state of consciousness were checked at half hour intervals, and a hundred cubic centimeters of fifty percent glucose solution was placed at the bedside for emergency administration. Lumbar puncture was deferred in order to avoid commitment to an operative course before studies were completed.

The patient's condition remained static until thee hours later when at four o'clock the blood pressure suddenly rose from 146/80 to 190/80. The pulse which had previously been 88 decreased to 80 per minute, an insignificant drop. The respirations suddenly increased to 44 per minute. The hypertonic glucose solution was administered intravenously, and a few minutes later respirations and the heart beat suddenly ceased. Within thirty minutes after the first change in blood pressure, the patient had succumbed before operation could be performed.

Post mortem examination showed no evidence of fracture of the skull. At the site of the right middle meningeal artery there was a large, bright red, freshly coagulated extradural hematoma, which extended throughout the right middle fossa compressing the temporal lobe (Fig. 1). The petrous portion of the temporal bone was covered by a gray purulent necrotic process which extended laterally and anteriorly to the foramen spinosum. The exudate seemed primarily to involve the area just above the semicircular canals, and a definite extension of the chronic middle ear infection

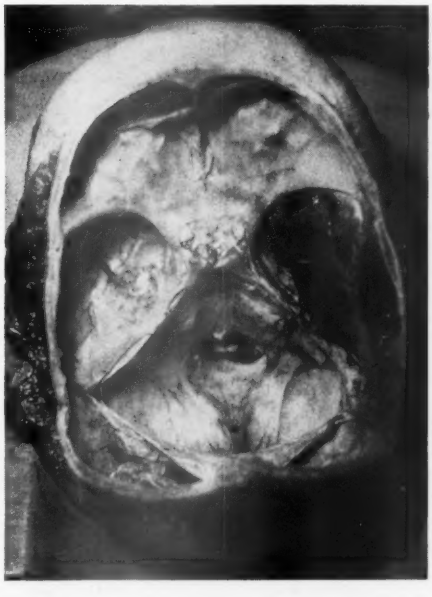

Fig. 1, Case 1.—J. Y. Massive extradural hematoma in the middle fossa.

was found in the osteomyelitic bone of the petrous ridge. The right cerebral hemisphere was swollen and edematous with flattening of the gyri and narrowing of the sulci. The right temporal lobe was compressed to about one half of its normal size by the hematoma. Congestion was observed over the left hemisphere and in the ependymal surface of the ventricular system, but no evidence of meningitis or brain abscess was found.

The pathological diagnosis was right middle meningeal hemorrhage, right chronic purulent otitis media and mastoiditis. (The bleeding point could not be demonstrated to our complete satisfaction, but the middle meningeal or internal carotid arteries were the most likely sources for a massive hemorrhage with such a rapid course.)

Comment: In retrospect there were two errors in the management of this case. First, there was the failure to consider that the intracranial lesion was anything but an inflammatory condition. The second mistake was not to appreciate fully the significance of a dilated homolateral pupil with bilateral extensor plantar reflexes. These are

the classical signs of temporal lobe herniation, a syndrome which is commonly seen in temporal extradural hematoma, temporal lobe abscess or tumor. In this case the hemorrhage must have followed erosion of a large artery because of the rapidly deteriorating course before there was any significant change in the blood pressure or pulse. At autopsy a bright red, well-coagulated hematoma was found, and although infection had occurred, there had been insufficient time for liquefaction of the clot, suggesting rapid progression of the lesion.

CASE 2.—J. M. L., 21 year old white male, was admitted to the Neurology Service at Crile Veterans Hospital, Cleveland, Ohio on June 30, 1949, with the history of fever, somnolence, mental confusion, and right fronto-temporal headache of five day duration. Just prior to his discharge from the Navy, five weeks previously the patient had developed a furuncle of the right ala nasi with associated swelling of the right infra and periorbital tissue and complete closure of the right eye. He was hospitalized for five days, received warm packs locally, and had intramuscular injections of procaine penicillin once a day for four days. Recovery was complete and the patient was well until the onset of his presenting symptoms.

Admission examination revealed a rectal temperature of 101,° nuchal rigidity, a suggestion of a left facial paresis, and equivocal bilateral Oppenheim reflexes, but otherwise the neurological examination was normal. Lumbar puncture disclosed a pressure of 230 mm of water; a few cc of clear, colorless fluid was removed. The fluid contained twenty-six lymphocytes and a total protein of 70 mg per hundred cc. A presumptive diagnosis of meningitis was made.

On the following day the patient was seen by the neurosurgical consultant who concurred in the above findings. A tentative diagnosis of right fronto-temporal brain abscess was made, and an electroencephalogram (Fig. 2) confirmed the presence of a lesion in that location. Blood and spinal fluid cultures were taken prior to administering drugs, and both were later reported as showing no bacterial growth. Beginning that evening 0.5 gm of aureomycin was given orally every three hours, and by July 4th the temperature had dropped to 99° rectally, but the patient had become more somnolent. The blood pressure had risen from 110/80 to 140/80, and the pulse rate dropped from 60 to 52 per minute. Although a dilated right pupil had developed, both pupils reacted to light, and there was still no evidence of choking of the discs. Minimal paresis was observed in the left upper extremity, and Oppenheim and Gordon reflexes were positive bilaterally although the Babinski was negative.

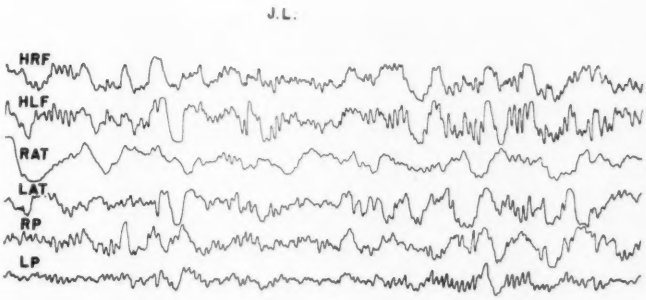

Fig. 2, Case 2.—J. L. Electroencephalogram showing delta or slow waves in the right anterior temporal region (third channel from top) suggesting a space taking intracranial lesion in that location.

With this evidence that a right temporal tentorial pressure cone was developing immediate operation was regarded as imperative. The similarity of this case to Case 1 was discussed. However, the presence of such a lesion was felt unlikely because of the rarity of this complication. The diagnosis of right fronto-temporal brain abscess was regarded as most probable. Preoperative skull x-rays showed a small circular area of rarefaction just above the frontal sinus about two centimeters from the mid-line. This was regarded as an osteomyelitic lesion or a venous lake. There was no calcification of the pineal gland.

Ventriculography was performed under local anesthesia on July 4 and a pronounced shift of the right lateral and third ventricles toward the left was demonstrated on the posterior-anterior view (Fig. 3). In the lateral view the right frontal horn was depressed and displaced backward by a massive lesion. A right fronto-temporal scalp flap was turned back and an osteoplastic flap sketched out. The first burr hole was placed over the rarefied area above the right frontal sinus. A large amount of dark bloody material with a slightly yellowish-gray tinge poured out. Cultures were taken. The surrounding bone was soft and necrotic, and the trephine hole was enlarged to remove this devitalized material and permit further examination of the area. About 150 cc of dark liquid blood was removed, and a large amount of extradural clot which was slightly adherent to the dura was scraped out. There was no evidence of membrane formation or marked degree of organization. On removing the hematoma numerous small oozing points were observed, no one of which could be definitely selected as the source of the massive

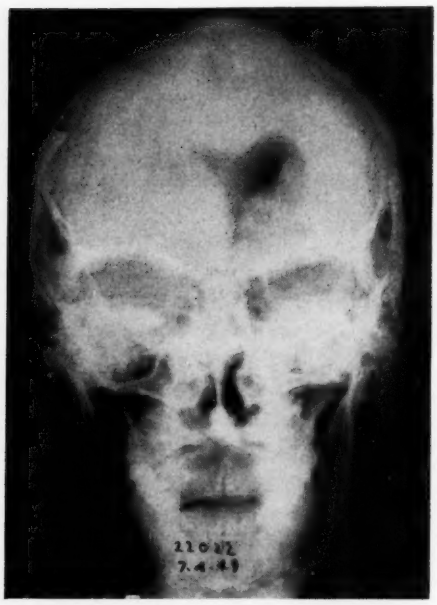

Fig. 3, Case 2.—J. L. Ventriculogram, anterior-posterior view, showing mass bulging into the right lateral ventricle and causing slight shift of the third ventricle from right to left.

hemorrhage. On careful examination no fracture of the skull was found. The dura was tacked up to the pericranium with stay sutures carefully placed through the outer layer of the dura. A soft No. 14 rubber catheter was left in situ at the base of the wound through which 500,000 units of penicillin were instilled and which also permitted adequate drainage.

Post-operatively the patient was placed on 100,000 units of penicillin intramuscularly, aureomycin 0.5 gm orally every three hours, and 1 gm of sulfadiazene with an equal dosage of sodium bicarbonate orally every four hours. One hundred thousand units of penicillin were instilled locally every three hours for the first two days, during which time the catheter remained in situ. A total of 11,700,000 units of penicillin were used intramuscularly and 1,200,000 units locally. Twelve grams of aureomycin were given pre-operatviely and 22.5 gm post-operatively to a total of 34.5 gm. Post-operatively the patient received 5 gm of sodium sulfadiazene

intravenously on the first day and an additional 44 gm orally thereafter making a total of 49 gm. All medication was discontinued by noon of July 16, twelve days postoperatively. The patient improved rapidly, and his convalescence was uneventful. The culture from the hematoma was reported as hemolytic staphylococcus aureus. A pneumoencephalogram was performed on July 23 to rule out a brain abscess, only minimal symetrical dilatation of the entire ventricular system was observed. The right frontal and temporal lobes had fully re-expanded. X-rays of the skull revealed a right frontal defect which was clean and showed no evidence of osteomyelitis. On July 28 the patient was discharged asymptomatic, neurologically negative, and with his wound well healed.

The patient was re-admitted for cranioplasty on January 9, 1950, but this was deferred due to sinusitis. During this admission he developed a convulsive seizure while asleep, and a repeat electroencephalogram showed focal epilepsy. He was dischargd on anticonvulsants, and re-admitted in March, 1950. At this time he had a second pneumoencephalogram which indicated a downward displacement of the right lateral ventricle. This was believed to be due to traction secondary to scar tissue. Six days later a tantalum cranioplasty was performed, and at that time the dura was opened and the right frontal lobe probed for a possible abscess. No pus was obtained, and it was observed that the brain pulsated freely and did not herniate. On March 17, 1950 the patient was discharged neurologically negative on an anti-convulsant regime.

After the discovery of the hematoma the patient was carefully questioned as to whether he had sustained any recent head injury. Apparently he had been knocked unconscious for an hour about six months prior to his illness, but had recovered rapidly without any neurological sequelae. All the large series of extradural hematoma published in the literature were checked for the longest recorded period between the time of injury and onset of the symptoms. The greatest intervals reported were: Munro 16 days;[18] McKenzie 21 days;[12] Moody 30 days;[15] and Gurdjian and Webster 31 days.[8] The presence of the grossly infected hematoma coupled with the long interval which had elapsed between the time of the head injury and his present illness, we believe justifies the assumption that the hemorrhage was secondary to the infectious process rather than due to the trauma six months prior to admission.

The successful outcome of this case rests on two factors: First, it was early recognized that this patient might have something other than a brain abscess because of the experience with Case 1. Second, the sigfinificance of the evidence of a temporal lobe pressure cone was

recognized early and acted upon immediately. The delay in development of the signs of hippocampal herniation would indicate that the source of this extradural hemorrhage was venous rather than arterial as it was in the first case.

COMMENT

There is a striking similarity between these two cases. Both patients had a massive extradural hemorrhage due to erosion of vascular channels by an infectious process having its origin extracranially. In both instances it was impossible to identify the source of the hemorrhage. In both cases there were signs of a tentorial pressure cone which are well known to neurological surgeons. As an expanding lesion displaces the temporal lobe downward and backward through the tentorium, it first exerts pressure upon the third nerve in its course along the base of the skull. The result is usually a homolateral pupillary dilatation. With further herniation of the temporal lobe the cerebral peduncle is compressed against the tentorium or the base of the skull laterally and inferiorly thus producing pyramidal tract signs on the opposite side. As the pressure increases edema becomes more marked and the opposite cerebral peduncle becomes involved so that there is the development of bilateral pyramidal tract signs. It is imperative to recognize these neurological signs early for they indicate an expanding temporal lesion which requires an immediate decompressive operation.

In 1929 Coleman[4] in discussing the indications for operation of patients with brain abscess states, "It is difficult to recognize the first stage of abscess and this is not of great importance surgically, because operation should not be done until after the formation of a capsule." McKenzie[13] and Grant[7] supported this concept in their discussions of brain abscess, but both carefully qualified their statements that drainage might have to be attempted if the patient became more comatose. At the present time a number of neurosurgeons follow this pattern of treatment and delay long enough to permit encapsulation of the suspected intracerebral lesion. From our experience with the two cases, which we have presented, we believe that it is dangerous to postpone operation in suspected cases of frontal and temporal lobe abscesses if the signs and symptoms of a tentorial pressure cone are developing.

The question may be raised as to why extradural hemorrhage has not been reported previously as a complication of infections of the nose and ears. We have sought in vain for a satisfactory explanation for the pathogenesis of this process, but thus far have been unable to find one.

It is well known that relatively trivial injuries to the head can cause intracranial hematomas. One might conjecture that these patients sustained forgotten minor head injuries, the infection being coincidental.

Both patients had received large doses of penicillin prior to admission. One may then speculate as to whether or not this might have had any influence on the situation. In a discussion of antibiotics Brunner[2] has commented, "Chemotherapy is of definite value in the treatment of intracranial complications; its influence in the prophylaxis of these complications is controversial. However, it is a fact that not infrequently chemotherapy of the primary condition alters the customary symptomatology and renders the diagnosis and treatment of intracranial complications more difficult than before the introduction of these new therapeutic agents." It is believed that infection may enter the bones of the skull by direct extension from sinuses to diploe or through the emissary veins of the sinus mucosa to the dural sinuses and then to the skull.[6, 14] Osteomyelitis develops and there is further progression of the process by thrombophlebitis of the venous channels of the diploe. The vessels then seal off gradually so that hemorrhage does not occur. It is thought that in some instances penicillin may be bacteriostatic and not bactericidal, and that perhaps infection may continue to smolder after the acute phase of the infection has been cleared up by chemotherapy. One would ordinarily suspect that a low grade infection would cause a laying down of fibroblastic elements with a tendency toward thrombosis of venous channels. However, this may no longer be as complete as it was prior to the day of antibiotics, and erosion of the vessel with hemorrhage may occur more easily.

SUMMARY

Massive extradural hemorrhage due to erosion of vessels by otological or rhinological infections is very rare. Two cases are presented in which this lesion was found.

Emphasis is placed upon the fact that a diagnosis of extradural hemorrhage as well as one of frontal or temporal lobe abscess must be considered in those cases of ear, nose, and sinus infections which exhibit a tentorial pressure cone. Early operation is essential if these patients are to survive.

No satisfactory explanation is given for the development of extradural hemorrhage in these patients. The question is raised as to whether the advent of penicillin has influenced the development of infection with some impairment of the customary thrombosis of

venous channels in the diploe of the skull. It is conceivable that this lesion may be found more frequently in the future because of the almost universal use of antibiotics in these infections.

The authors wish to thank Dr. Claude S. Beck, Senior Neurosurgical Consultant, Crile Veterans Administration Hospital, Cleveland, Ohio for the opportunity of presenting the second case for publication.

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XVII

THE USE OF ANTIBIOTICS IN OTOLARYNGOLOGY

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During the past two years clinical observation has made me increasingly aware of the fact that I was not seeing as satisfactory response to the use of penicillin as I had observed previously. In an effort to substantiate and explain this clinical impression, I reviewed some of the charts of patients with sinus infection who had cultures from pus in the nose made on penicillin sensitivity plates during the past six years. The information obtained was rather startling, as is shown in Table I.

TABLE I.

CULTURES FROM PUS IN THE NOSE IN CASES OF ACUTE OR CHRONIC SUPPURATIVE SINUSITIS.

Blood Agar Plates Treated with Penicillin.

YEAR	NUMBER OF CULTURES	GRAM POSITIVE COCCI ONLY
1945	10	80% sensitive to 0.2 unit per cc (inhibited by)
1946	44	82% sensitive to 0.2 unit per cc
1947	33	60% sensitive to 0.2 unit per cc
1948	46	26% sensitive to 0.2 unit per cc
1949	48	12% sensitive to 0.2 unit per cc
1950	50	0% sensitive to 0.2 unit per cc

These data may possibly reflect unintentional selection of cases because most of the patients from whom these cultures were made had been treated with penicillin before being referred to us.

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Read at the 36th Annual Clinical Congress of the American College of Surgeons, Boston, Mass., October 25, 1950.

My interpretation of the data in Table 1 is as follows: because of the widespread use of penicillin as dust, as nose drops, as aerosol inhalations, and inadequate dosage by mouth or by injection, the more sensitive strains have been killed and the resistant strains have survived to be passed on to friends and relatives. Thus in a period of four short years, the bacterial flora of the upper respiratory tract has become relatively resistant to the action of penicillin.

Fleming[1] said in 1946, "It is to be hoped that penicillin will not be abused as were the sulfonamides. . . . It is the administration of too small doses which leads to the production of resistant strains of bacteria, so the rule in penicillin treatment should be to give enough."

Pus for these cultures was obtained from the interior of the nose by means of a suction collector. The organisms demonstrated were various types of staphylococci, streptococci and pneumococci, grown on blood agar plates treated with several concentrations of penicillin, with one untreated control plate. I am not stating that these cultures represent the infecting organism, the pathogen solely responsible for the disease, but they do represent the bacterial flora found in pus in the noses of patients having obvious suppurative sinus infection, and show the decreasing sensitivity of these organisms to the action of penicillin.

My belief that the gram positive cocci demonstrated by these cultures are at least some of the pathogens is strengthened by the

TABLE II.

1950 SENSITIVITY CULTURES FROM PUS IN THE NOSE IN A CASE OF CHRONIC SUPPURATIVE SINUSITIS.

	Penicillin			Dihydrostrepto-mycin			Aureomycin			Terramycin		
	1	3	5	5	10	25	1	2	5	1	2	5
Hemolytic coagulase-positive staphylococci	4+	4+	4+	0	0	0	0	0	0	0	0	0
Beta Hem. Strep.	0	0	0	4+	3+	0	0	0	0	0	0	0

Penicillin in units per cc. Dihydrostreptomycin, aureomycin and terramycin in mcg per cc.

4+—heavy growth. 0—no growth.

Smears showed many gram positive cocci.

smears which show many cocci mixed with the neutrophils. Quite often two organisms, usually a staphylococcus and a streptococcus, were found in a given sample of pus, and their behavior with respect to penicillin sensitivity plates varied considerably, as is shown by Table II.

Nichols and Needham[2] using this same type of sensitivity culture in 1949, found that 34 out of 50 strains of staph. aureus required more than 1.6 units of penicillin to inhibit their growth.

As Mosher[3] has stated—determination of the sensitivity of the causative bacteria may be the most vital point in the use of chemotherapy and it does away with the old method of trial and error.

TABLE III.

JANUARY AND FEBRUARY, 1950, CULTURES.
GRAM POSITIVE COCCI ONLY.

	PENICILLIN					
	1.0 unit per cc		3.0 units per cc		5.0 units per cc	
	Growth	No growth	Growth	No growth	Growth	No growth
Hem. staph. aureus (10 strains)	10	0	9	1	6	4
Staph. aureus (21 strains)	21	0	16	5	13	8
Strep. viridans (13 strains)	11	2	11	2	8	5
Beta Hem. strep. (6 strains)	4	2	2	4	2	4
Totals (50 strains)	46	4	38	12	29	21
Gram + cocci % inhibited		8%		24%		42%

Table III shows the behavior of the gram positive cocci on penicillin treated blood agar plates in 1950.

These data cast doubt on the current idea that an intramuscular injection of three or four hundred thousand units every 24 hours will be effective as treatment for most respiratory infections, and make ludicrous the reference to 0.03 unit as the "minimal effective therapeutic level."

The clinical evidence of the necessity for using big doses of penicillin is present in the case reports of patients who were cured with large doses after small doses had failed, and we have many case reports showing this sequence.

Even the pneumococcus has become more resistant, so that in 1950 it frequently grows on plates containing 1 unit of penicillin per cc.

It is unfortunate that penicillin doses are not prescribed in grams instead of units. A million units sounds like such a tremendous dose that one hesitates to give more. Five million units weighs approximately three grams and at least this much must be administered daily to maintain a serum concentration of five units.[4]

Obviously, natural resistance plays a major role in control of all infections and *if resistance is good, relatively small doses of any antibiotic may be effective.* Those interested in a comprehensive presentation of this subject are urged to read "Natural Resistance and Clinical Medicine" by Perla and Marmorston.[5]

The following quotation from Sir Alexander Fleming's book entitled, "Penicillin, Its Practical Application,"[6] should serve to keep our thinking straight: "There are a few simple rules for the use of penicillin in treatment of bacterial infections. These may seem too simple—even childish—but experience in watching penicillin being used has made it clear that these rules are often broken with resulting disappointment.

"1. It should be used only when there is an infection by a penicillin-sensitive microbe.

"2. Penicillin must be administered in such a way that it comes in contact with the infecting microbe.

"3. The dose should be such that *in the infected area* the concentration of penicillin is sufficient to destroy the bacteria.

"4. The treatment should be persisted in until the infection is defeated."

These rules were repeated in the (1950) second edition of his book.[7]

Regardless of the numerous articles advocating the topical use of penicillin as nose drops, as aerosol inhalations, by injection into antra and by displacement, the words of Dr. Fleming have led me to ignore these methods because they do not adequately live up to his second and third rules. Since penicillin must be administered in such a way that it comes in contact with the infecting microbe, and

because the germs are located at various depths within the tissues where they can be reached only by blood-borne penicillin, I use only intramuscular injections.

Furstenberg[8] voiced the same opinion in 1949, and pointed out that ciliary action will carry away any topically applied antibiotic before it has had time to be effective.

Leo Loewe[9] sometimes uses 40 million units daily in treatment of subacute bacterial endocarditis. I see no reason why we should not follow his example and really cure many of our patients having chronic sinus infections, who in the past would have been subjected to multiple sinus operations. Because of Loewe's conviction regarding the efficacy of large doses when smaller doses had failed, he was able to report 81% cure of 33 treatment failures from other institutions.

Quoting Marvin,[10] "Loewe deserves great credit for having demonstrated the value of large doses of penicillin for subacute bacterial endocarditis after the Penicillin Committee had officially declared it to be of no value."

In my experience, the use of large doses does not increase the incidence of allergic reactions to penicillin. Allergic reactions have been infrequent and when present have responded promptly to use of procaine intravenously or to cortisone intramuscularly.

The site of the infection as well as the degree of penicillin-sensitivity of the organism will partially determine the duration of treatment as is indicated in Table IV, taken from Fleming's book[6] published in 1946.

TABLE IV.

AVERAGE MINIMUM DURATION OF DAYS OF TREATMENT FOR PATIENTS RECEIVING 60,000 UNITS EVERY THREE HOURS.

Uncomplicated gonorrhea	1 day
Vincent's angina	2 days
Erysipelas, impetigo	3 days
Carbuncles, cellulitis	5 days
Breast abscesses	7 days
Otitis media and mastoiditis	8 to 10 days
Sinusitis	10 to 12 days
Complicated septicemias	12 to 21 days
Endocarditis	21 to 28 days

I think this table is important because it indicates that otitis media and sinusitis can be almost as difficult to cure as complicated septicemias and endocarditis. Obviously there is something about infections in bone surrounded cavities which makes them respond poorly and slowly to average doses of penicillin. Probably it is the fact that inflammatory swelling of soft tissues surrounded by bone constricts the blood supply to these tissues. I agree with Eagle[11] and his associates who suggest that "a large dose may promote the penetration of penicillin into walled-off foci of infection which are only slowly equilibrated with the tissue fluids, and into which penicillin might not diffuse in adequate concentration after a small dose which provides a low 'head of pressure' for a relatively brief period." It is with this thought in mind that I am using "fortified" procaine penicillin and the results seem to support Eagle's theory.

When penicillin-resistant infections are encountered, one naturally thinks of other antibiotics. We started making cultures on streptomycin-treated plates in October, 1947, using 5, 10 and 25 micrograms per cc. As soon as dihydrostreptomycin became available, sensitivity cultures were made with this antibiotic and we found that its antibacterial effect with reference to the cocci was the same as that of streptomycin.

Keefer and Anderson[12] indicate that dihydrostreptomycin is as effective as streptomycin, is less toxic and is less apt to produce hypersensitive reactions.

TABLE V.

JANUARY AND FEBRUARY, 1950, CULTURES.
GRAM POSITIVE COCCI ONLY.

	DIHYDROSTREPTOMYCIN					
	5 mcg per cc		10 mcg per cc		25 mcg per cc	
	Growth	No growth	Growth	No growth	Growth	No growth
Hem. staph. aureus (10 strains)	4	6	3	7	2	8
Staph. aureus (21 strains)	5	16	5	16	3	18
Strept. viridans (13 strains)	7	6	7	6	3	10
Beta Hem. strep. (6 strains)	6	0	4	2	3	3
Totals (50 strains)	22	28	19	31	11	39
Gram + cocci % inhibited		56%		62%		78%

The effectiveness of dihydrostreptomycin shown by Table V has led me to use it for some infections due to the cocci and the clinical results parallel the laboratory data. In serious infections due to cocci, I use dihydrostreptomycin and penicillin simultaneously.

In vitro studies by Jawetz[13] and his associates have shown that mixtures of streptomycin and penicillin have a synergistic action against enterococci and indicate that the rapid bactericidal effect of the streptomycin-penicillin mixtures represents at least a 10-fold potentiation of penicillin action.

According to Crofton,[14] in non-tuberculous infections a continuous blood level of streptomycin is important and injections should be given every six hours. A dose of ½ gm will give a maximum blood level of 15-30 mcg per cc, falling to 4-8 mcg per cc at the end of six hours.

According to Carr[15] and his associates, 1 gm of dihydrostreptomycin intramuscularly produces a serum concentration between 45.6 and 57.6 mcg per cc one hour after injection in patients with normal renal function. The maximum non-toxic concentration of dihydrostreptomycin in the blood serum is not yet known. Carr states, "We have shown that 1 gm of dihydrostreptomycin every 12 hours is a safe dose for an adult who weighs 50-75 kg if renal function is normal. . . . It would seem, therefore, that neurotoxic reactions to dihydrostreptomycin might be avoided or minimized by regulating the dose so that the maximal concentration in the blood serum is never more than 50 mcg per cc."

Because our cultures have shown that lower concentrations are effective against the gram positive cocci and because serum concentrations begin to fall sharply after six hours, as was shown by Levin and his associates,[16] it has been our practice to give ½gm every six hours.

Delayed loss of hearing due to dihydrostreptomycin was reported by Allison and associates[17] in July, 1949.

Recent information obtained from Glorig[18] also indicates that dihydrostreptomycin can have a delayed toxic effect on the cochlear division of the VIIIth nerve. Sixteen percent of 32 patients given 2 gm of dihydrostreptomycin daily for at least 43 days had severe hearing loss. I have one patient who received only 22.6 gm of dihydrostreptomycin who developed high tone perceptive hearing loss and severe persistent tinnitus two months later; hence we must be cautious in administration of dihydrostreptomycin and be certain that renal function is not impaired.

Glorig[19] points out that streptomycin is probably the drug of choice when long term treatment is indicated, because it is better to risk the loss of vestibular function than to risk the loss of cochlear function. I have discontinued the use of dihydrostreptomycin.

The results of our aureomycin sensitivity cultures are shown in Table VI.

TABLE VI.

JANUARY AND FEBRUARY, 1950, CULTURES.
GRAM POSITIVE COCCI ONLY.

	AUREOMYCIN					
	1 mcg per cc		2 mcg per cc		5 mcg per cc	
	Growth	No growth	Growth	No growth	Growth	No growth
Hem. staph. aureus (10 strains)	3	7	1	9	1	9
Staph. aureus (21 strains)	5	16	1	20	0	21
Strept. viridans (13 strains)	7	6	2	11	1	12
Beta Hem. strep. (6 strains)	4	2	2	4	1	5
Totals (50 strains)	19	31	6	44	3	47
Gram + cocci % inhibited		62%		88%		94%

Quoting Kirby,[20] "In contrast to penicillin, the action of the three new antibiotics is primarily bacteriostatic rather than bactericidal. This probably accounts for the relatively poor results obtained with aureomycin and chloramphenical in the treatment of subacute bacterial endocarditis, despite the high degree of in vitro susceptibility of the etiologic organisms." Admittedly sensitivity cultures of the type I am reporting indicate bacteriostatic and not bactericidal effect.

According to Herrell and Heilman,[21] the serum concentration of aureomycin begins to diminish six hours after an oral dose, so it has been my practice to give doses at six hour intervals. Herrell and Heilman state that a serum concentration between two and four micrograms can be maintained by giving 750 mg of aureomycin by

mouth every six hours; therefore, I have used this dose and interval when aureomycin appeared to be the drug of choice. It may produce nausea, vomiting and diarrhea, or induce development of monilial infections, so there are some relative contraindications to its use.

Our cultures (Table VII) indicate that chloromycetin is not as effective as aureomycin against the gram positive cocci and for this reason I have not used chloromycetin in treatment of otolaryngologic infections.

TABLE VII.

JANUARY AND FEBRUARY, 1950, CULTURES.
GRAM POSITIVE COCCI ONLY.

	CHLOROMYCETIN					
	1 mcg per cc		2 mcg per cc		5 mcg per cc	
	Growth	No growth	Growth	No growth	Growth	No growth
Hem. staph. aureus (10 strains)	9	1	9	1	7	3
Staph. aureus (21 strains)	14	7	11	10	7	14
Strept. viridans (13 strains)	9	4	8	5	2	11
Beta Hem. strep. (6 strains)	5	1	4	2	1	5
Totals (50 strains)	37	13	32	18	17	33
Gram + cocci % inhibited		26%		36%		66%

I no longer use sulfadiazine except for meningitis. The superiority of penicillin over sulfadiazine was shown by Wilcox[22] and in 42 percent of his well studied cases of otitis media the use of sulfadiazine was discontinued because of toxic symptoms or failure to cure the infection.

Table VIII gives a quick comparison of the behavior of the gram positive cocci on blood agar plates treated with four antibiotics. These concentrations of each antibiotic were selected because I thought they were fairly close to the serum concentrations produced by small, medium and large doses of the drug in question.

TABLE VIII.

JANUARY AND FEBRUARY, 1950, SENSITIVITY CULTURES FROM PUS IN THE NOSE

50 Cultures	PENICILLIN		
	1 unit per cc	3.0 units per cc	5.0 units per cc
% gram positive cocci inhibited	8%	24%	42%
	DIHYDRO-STREPTOMYCIN		
	5 mcg per cc	10 mcg per cc	25 mcg per cc
% gram positive cocci inhibited	56%	62%	78%
	AUREOMYCIN		
	1 mcg per cc	2 mcg per cc	5 mcg per cc
% gram positive cocci inhibited	62%	88%	94%
	CHLOROMYCETIN		
	1 mcg per cc	2 mcg per cc	5 mcg per cc
% gram positive cocci inhibited	26%	36%	66%

Table IX gives a comparison of another set of cultures made during the summer of 1950. It indicates that terramycin is more effective than aureomycin against the gram positive cocci. We have had too few cases treated with terramycin to be certain about the comparative merits in treatment of infections, but I can report that terramycin seems to cause nausea, vomiting and diarrhea less frequently than does aureomycin.

Herrell[23] and associates have shown that giving 1.0 gm of terramycin every six hours will usually produce a serum concentration between 4 and 8 mcg per cc.

As treatment for acute otitis media I use 3 or 4 gm daily in divided doses.

In my opinion, acute sinusitis accompanied by either fever or pain warrants treatment with one of the antibiotics. Chronic sinusitis is the result of neglected or inadequately treated acute sinusitis, hence acute sinusitis should be treated with antibiotics in doses large enough to produce prompt cure. In my experience, procaine peni-

TABLE IX.

JUNE AND JULY, 1950, SENSITIVITY CULTURES FROM PUS IN THE NOSE.

25 Cultures	PENICILLIN		
	1 unit per cc	3 units per cc	5 units per cc
% gram positive cocci inhibited	8%	40%	56%
	DIHYDRO-STREPTOMYCIN		
	5 mcg per cc	10 mcg per cc	25 mcg per cc
% gram positive cocci inhibited	40%	60%	76%
	AUREOMYCIN		
	1 mcg per cc	2 mcg per cc	5 mcg per cc
% gram positive cocci inhibited	64%	72%	84%
	TERRAMYCIN		
	1 mcg per cc	2 mcg per cc	5 mcg per cc
% gram positive cocci inhibited	68%	84%	92%

cillin 4.8 million units daily, or aureomycin or terramycin 3 gm. daily usually gives satisfactory results. Treatment should be continued for 7 days. If the patient does not show good response within 48 hours or if intracranial complications threaten, one of the other antibiotics in full dose should be added to the treatment program. Some of our best results have been obtained by using dihydrostreptomycin 0.5 gm every six hours and fortified procaine penicillin 400,000 units every three hours for periods of 7 to 10 days. According to Nichols,[24] in vitro experiments show definite synergism between penicillin and streptomycin.

External surgical drainage of acute frontal sinusitis is still necessary in rare cases.

Chronic sinusitis often requires larger doses if one hopes to achieve a cure without surgery. In some of our cases the infection cleared up with doses of fortified procaine penicillin as large as 6.4 million units daily after smaller doses had failed.

The following report illustrates what may be accomplished by large doses in some cases of sinus infection.

REPORT OF A CASE

M. P., female, age 39. Her chief complaints were yellow nasal and post nasal discharge for 24 years and chronic productive cough since she had severe pneumonia and scarlet fever at the age of 15 years. She produced two to four ounces of purulent sputum every 24 hours, and had recurrent bouts of hemoptysis. A bronchogram demonstrated bronchiectasis involving all lobes except the right upper. Her cough decreased moderately while receiving procaine penicillin 600,000 units every 6 hours for seven days. She then was treated with fortified procaine penicillin 600,000 units every three hours for a period of 7 days. The sinus infection cleared up completely and her daily sputum decreased to 2 drams of non-odorous, mucoid secretion. Her weight increased from 112 to 123 and she said her health was the best it had been in 20 years. Her improvement has been maintained.

Puncture and lavage of pus-filled antra is always indicated. In cases of chronic sinusitis minimal intranasal surgery, such as removal of polyps and intranasal antrostomy can well be combined with antibiotic therapy.

Results of antibiotic therapy for otitis media are easier to evaluate than the results for sinus infections. Acute otitis media warrants adequate antibiotic therapy and the doses we use are similar to those advocated for acute sinusitis. Treatment should be continued for at least 48 hours after the discharge from the middle ear has ceased. Early myringotomy is still an important part of the treatment. Myringotomy promptly relieves pain and evacuates the exudate, which if allowed to remain in the middle ear, will organize and cause permanent hearing loss.

The influence of antibiotics on the incidence of acute mastoid surgery at the Geisinger Memorial Hospital is shown in Table X.

TABLE X.

DECREASING INCIDENCE OF "SIMPLE" MASTOID OPERATIONS AT THE GEISINGER HOSPITAL.

Year	Period	No. cases acute otitis media and mastoiditis	No. "simple" mastoid operations	Percent requiring mastoidectomy
1937	Pre-sulfa	202	119	58.9%
1943	Sulfa	282	74	26.2%
1946	Small dose penicillin	247	10	4.0%
1949	Large dose penicillin	189	5	2.7%
1st 6 mos. 1950	Larger dose penicillin. Resistant organisms.	93	5	5.3%

The decreasing incidence of mastoid operations has not resulted in an increasing incidence of complications.

Our case histories repeatedly show that 300,000 or 400,000 units daily are not enough to cure many cases of acute otitis media. Another fact that is apparent is the number of relapses that occur when treatment is stopped after 3 or 4 days.

Antibiotic therapy of chronic middle ear or mastoid infections is seldom effective.

Acute pharyngitis and acute tonsillitis respond rapidly to smaller doses than are necessary for acute middle ear infections.

Acute supraglottic laryngitis often called acute epiglottitis, is frequently due to h. influenzae and hence dihydrostreptomycin should be given as well as penicillin in large dose. Twenty mg per pound body weight per day is usually an adequate dose of dihydrostreptomycin for a child. Our penicillin dose for these children is usually 400,000 units of fortified procaine penicillin every 6 hours. These same doses are used for children having acute subglottic laryngitis, more commonly known as acute laryngotracheobronchitis. For these serious fulminating infections it is best to rely on antibiotics given by intramuscular injection, because this insures rapid and complete absorpton of the drugs given. It is very difficult to give an intravenous injection to a restless, dyspneic child.

CONCLUSIONS

1. Sensitivity cultures on blood agar plates are a useful method of determining which antibiotic to use and the size of the dose necessary to promptly cure the infection.

2. The gram positive cocci causing otolaryngologic infections have become relatively resistant to the action of penicillin.

3. Many of these infections require daily doses of penicillin between 3 and 6 million units.

4. Doses of this magnitude can be given as fortified procaine penicillin 400,000 or 800,000 units intramuscularly every 3 hours.

5. Severe infections respond more quickly if the patient is also given streptomycin 0.5 gm. intramuscularly every 6 hours.

6. Topical applications of antibiotics have little value.

7. Aureomycin and terramycin given in daily dose of 3 or 4 grams are effective drugs for treatment of infections due to many of the gram positive cocci if vomiting or diarrhea do not interfere with their absorption.

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XVIII

PRIMARY INTRANASAL NEUROBLASTOMA

REPORT OF 3 CASES

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AND

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Clinicians and pathologists are familiar with neuroblastomas as they occur in the adrenal gland and sympathetic ganglia and their common metastatic syndromes involving the skull (Hutchinson's) and liver (Pepper's)[1] as well as their counterpart in the eye, the retinoblastoma. There is however a very scanty literature and even less knowledge concerning what has been termed by European authors "esthesio-neuroblastoma" of the nose. These tumors have originated independently in the nasal fossa, unrelated to the central nervous system and visceral tumors, are often malignant; more frequently, as in the present cases, benign; appear only in the adult and present at first examination the clinical appearance of a bleeding nasal polyp.

In a review of the available literature on intranasal nerve tumors there were several reports covering glioma[2] neurofibroma, ganglioneuroma and meningioma[3] in American and English journals but none have mentioned neuroblastoma. The collection of cases and attempts to classify these tumors has been done primarily by French authors beginning in 1924[4] with several additional reports from Portuguese and Italian schools. This European group recognized that these tumors arise independently from the central nervous system, coming from the olfactory placode, the primordium of the later olfactory mucosa and consider them tumors "sui generis" and quite malignant.[5]

Though in the total literature pertaining to intranasal nerve tumors there have been some forty-odd cases reported, to date only

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14 primary neuroblastomas or, according to their degree of differentiation, "esthesio-neuro-epitheliomas" have been described, entirely in European literature: 5 cases by Portmann and Beillard,[6] 4 cases by Travares,[7] and one case each by da Costa,[8] Jemmi,[9] Wohlwill,[10] Eigler,[11] and Martin, et al.[12]

Since 1947 there have been three cases of intranasal nerve tumors in the Massachusetts Eye and Ear Infirmary in which the pathological diagnosis has been "neuroblastoma," and in which no other site of origin has been found. All three patients are living at present writing.

CASE REPORTS

CASE 1.—Mrs. L. L., aged 76, was seen in the emergency ward for her first nosebleed from the left side on May 20, 1947. She had been under prior treatment by her physician for asymptomatic hypertension. The admission blood pressure was 170/80. After clot aspiration two bleeding points on the lateral nasal wall were cauterized with 50 percent trichloracetic acid. Because of recurrent epistaxis from the left nostril she was admitted to the ward the following day with a blood-pressure of 208/94 and vaseline packs were inserted to control the hemorrhage. Two days later after the packs were removed examination of the left ethmoid region and nasal cavity revealed a nodular, reddish mass suggestive of neoplasm. A portion of the polypoid mucous membrane was removed for pathological examination. Removal of the specimen was followed by profuse hemorrhage easily controlled with thrombin and gel-foam. Routine blood and urine examination was negative.

The tissue was fixed with Helly's solution and stained with Mallory's phosphotungstic acid hematoxylin, Foot, Cajal, Hematoxylin and Eosin stains. The specimen was a 0.5 cc of nasal polyp. The epithelium is respiratory in type at two sections while between them it is a low stratified type; at the opposite edge of the section there are spicules of bone. There is scanty stromal tissue but a great number of capillaries and larger vessels are seen scattered throughout the tissue dividing the tumor cells into large groups of various size. In one portion there is a large collection of lymphocytes interspersed between the cords and masses of tumor cells.

Collagen stains show that there is very little of this material present and none in the actual tumor itself. There is scanty reticulum unrelated to the tumor cells and their processes.

The nuclei stand out clearly from the faint hazy background substance that resembles ground glass. This substance took neither collagen nor neurofibril stains. No distinction of a cell outline or cytoplasm could be determined. The nuclei average 12 to 16 μ in diameter, are round or oval with finely granular chromatin material rather evenly dispersed; usually two to four larger chromatin granules are seen in each nucleus (Fig. 1). No mitoses are seen. The diagnosis is Neuroblastoma.

CASE 2.—Miss F. G., aged 22, was admitted on Feb. 6, 1948, with a diagnosis of acute left ethmoiditis. The past history revealed that in 1942 she was unable to breathe through her left nostril and had several polypi removed. A year or so later x-ray examination was made (results unknown) and she had what was apparently an external antrotomy and again polypi were removed.

In 1946 after an automobile accident and after wearing a feeding tube for several weeks the left side of her face became swollen and she developed more intranasal polypi. The left-sided swelling disappeared under sulfonamides and

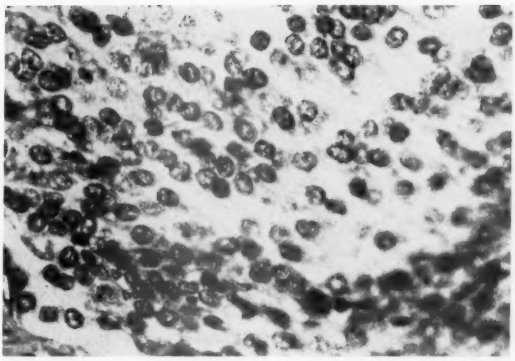

Fig. 1.—Nuclei in specimen from Case 1. Magnification: 850 times.

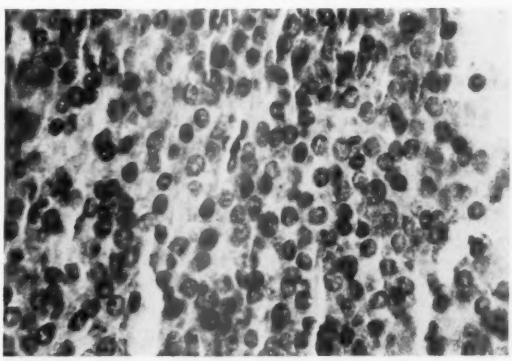

Fig. 2.—Nuclei in Case 2, showing chromatin granules. Magnification: 850 times.

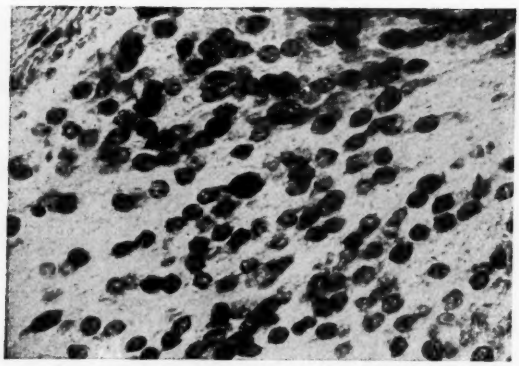

Fig. 3.—Nuclei of slightly varying size in Case 3. Magnification: 850 times.

more polypi were removed. X-ray treatments were given which did not help. Just before Christmas of 1947 she had more x-ray therapy.

Admission examination revealed that the left norstril was blocked by a bleeding traumatized polyp. The left inferior turbinate had been previously removed. On Feb. 7, 1948 under gas-oxygen-ether anesthesia an intranasal ethmoidectomy was performed with removal of a large granulation from the depths. The left antrum was found to be small. The ensuing bleeding was profuse but controlled by packing the exenterated labyrinth. Healing was uneventful and she was discharged well on the eighth day. She has had no further intra-nasal complaints.

The Microscopical description of tumor, fixed with Helly's solution and stained with Mallory's phosphotungstic acid hematoxylin follows. The specimen is a piece of tissue one centimeter square covered with respiratory epithelium, replaced in certain sections by a stratified squamous type. In the scanty stroma and just beneath the epithelium are seen numerous serous glands and their ducts. The tumor nuclei as in Case 1 are distinct and arranged in masses and cords, the cytoplasm again is sparse and difficult to discern, the fibrillar background is likewise hazy and did not take collagen stain. The size of the nuclei is about the same as in Case 1 (Fig. 2) perhaps smaller; round and oval-shaped with finely granular chromatin and several larger chromatin masses in each nucleus. Mitoses are absent. The diagnosis is Neuroblastoma.

Case 3.—Mrs. A. G. R., aged 57, was first seen by a physician sometime in the fall of 1949. At this time he removed some polypi from the right nasal fossa. The diagnosis by the Tumor Diagnostic Service at the Harvard Medical School was "neuroblastoma." She was admitted to the Massachusetts Eye and Eye Infirmary on January 30, 1950. The anamnesis revealed that for the past six months she had had tinnitus and headache of a throbbing character. Since November of 1949 she had complained of profuse watery nasal discharge and of a blocked right nostril. At that time another doctor removed some polypi but did not send any specimens for pathological examination.

She had had many complaints including "sinus trouble" all her life. One significant fact was that she had noticed some vague prickling sensations across

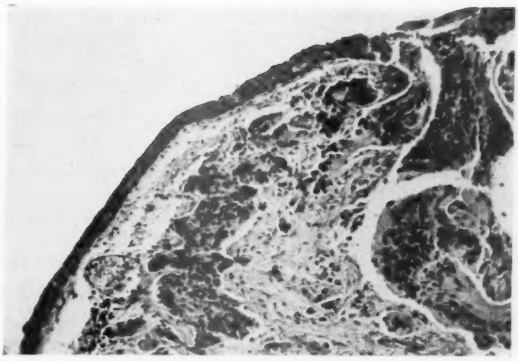

Fig. 4.—Edge of tumor in Case 3, showing pseudo-rosette formation, a thin stroma and low stratified squamous epithelium. Magnification: 425 times.

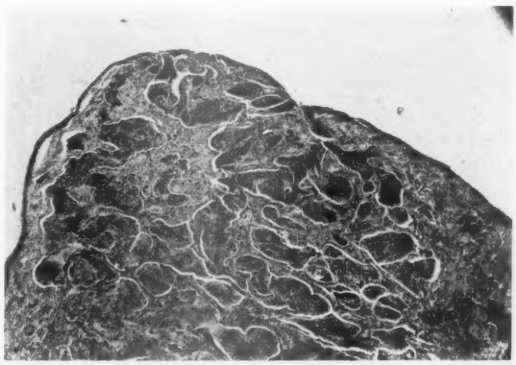

Fig. 5.—Low power 85 times showing masses of tumor cells interlacing with each other.

the right side of her face in the past several weeks. Examination showed a large new growth in the right nostril. X-rays revealed very little involvement of the ethmoid sinus and none of the right frontal or the antrum.

Through a lateral rhinotomy complete exenteration of the right ethmoid was carried out. Several easily bleeding polypi were removed; the actual tumor masses themselves were firm, reddened polypi, freely bleeding and very different from the usual cystic masses to be expected in long standing sinus disease.

The specimen was fixed in Formalin-Zenker's fluid and stained with Hematoxylin and Eosin, Bodian.

The specimen consisted of a cubic centimeter of tissue containing irregularly distributed masses of basophilic-staining nuclei of fairly uniform size (Fig. 3). The tumor strands and masses take up most of a polyp covered by normal respiratory epithelium. Very little of the original stroma remains. In a small portion of the specimen opposite the epithelium are a few normal bone spicules. More than the usual number of lymphocytes are seen distributed among the tumor clumps. In several areas there is frank extravasation of red cells; in other fields there is an actual increase in new vessel formation consisting of endothelial lined spaces filled with blood. Beneath the epithelium in the thin stroma are a few mucous glands and ducts. In one section of the specimen are a few masses of tumor nuclei arranged in a pseudo-glandular rosette formation (Fig. 4). The nuclei average about 12 μ to 14 μ in diameter, are round vesicular with finely granular and evenly distributed chromatin. The cytoplasm is scanty. The nuclei tend to arrange themselves in large masses: some tear-shaped, others club-shaped, the fibrillar network in which they are embedded usually streaming from one side of each mass and joining or interlacing with the others (Fig. 5). This material did not take silver stain well. Here and there a mitosis is to be found. The diagnosis is Neuroblastoma.*

DISCUSSION

To the fourteen previously reported cases of intranasal neuroblastoma three new ones are now added. With the exception of Case 3 which is probably malignant by position only, they have been found benign. All were in females and no site of origin other than the nose was discovered clinically. Grossly the tumors presented the appearance of obstructing nasal polypi; Case 1 was first diagnosed on admission as a nosebleed, Case 2 as acute ethmoiditis, and Case 3 as nasal polypi without epistaxis. The polyps in these cases were not the usual mucoid polypi seen in cases of long standing infection or of allergy, but were rather more firm, darker and redder in color, in one case at least with a definite tendency to bleed easily when touched. This clinical appearance has prompted the routine biopsy and on occasion the removal of such polypi for microscopic

*Dr. Tracy Mallory made the original diagnosis in cases 1 and 2, Dr. Shields Warren in case 3. Other pathologists who have examined the slides and expressed interest in them are Drs. Benjamin Castleman, Sidney Farber, David Freiman, Olive Gates, and Charles Kubik. To them grateful thanks is expressed for their advice and criticism, however full responsibility for the foregoing descriptions and presentation rests solely on the junior author. One pathologist while examining the slides remarked that microscopically they were enough alike to have come from the same patient.

examination as they have been found usually to be tumors of so widely varying types, as papillary carcinoma, melanotic sarcoma, hemangioma, meningioma, and neurogenic sarcoma. In fact, these unusual tumors are seen frequently enough to warrant the routine microscopical examination of all polypi removed at operation.

It would appear from their site of origin, high on the lateral nasal wall in relation to the ethmoid labyrinth and apparently unrelated to the central nervous system, that these tumors do in point of fact arise from the olfactory mucous membrane. According to Maximow and Bloom[15] the olfactory region is found in embryos of 4 weeks or 4.9 mm as paired, thickened *ectodermal* areas at the anterior edge of the medullary plate. These are known as the olfactory placodes. Their structure at this time is similar to that of the medullary epithelium. The plates are later gradually invaginated and recede from the surface. Some epithelial cells are transformed into olfactory elements which send axons growing toward the anterior part of the brain vesicle. Tumors arising from this area would be of ectodermal origin and similar in all respects to those derived from the neuroectoderm forming the central nervous system and sympathetic ganglia.

In contrast to this view is the one expressed by Berger, Luc and Richard[4] who described "the first case of a neoplasm of the olfactory placode." They considered that this placode was of endodermal origin and could give rise to tumors independent of the central nervous system as well as of the sympathetic system. The supporting cells and the neurocytes of the olfactory membrane originate from the same stem cell, the "esthesio-neuroblast;" when differentiation into the two types of cells occurs there results the esthesio-neuroepithelioma composed on the one hand of epithelial elements grouped in rosettes and equivalent to the cylindrical supporting cells of the olfactory membrane, and on the other hand of neurocytes arranged in cords and masses with neurofibrillar elongations; thus having morphological traits in common with neuroepitheliomas and sympathomas. When only neurocytes differentiate, the result is the esthesio-neuro-cytoma; if neuroblasts only proliferate, the result is the esthesio-neuroblastoma. Berger notes that other authors tend to include these two with the group of sympathomas, but he opposes this, saying that the supposed nasal sympathomas are actually placodial tumors.

Escat,[13] Portmann and Beillard,[6] however have reported three cases of nasal sympathomas and suggest the hypothesis that they arise from the small sympathetic fibers of the nasal mucosa and of the sphenopalatine ganglion and are therefore of neuroectodermal origin.

From the practical standpoint these two opposing views are of minor importance; however, if the tumors in question arise from the olfactory placode they are, according to Berger, of endodermal origin; if of sympathetic origin they are essentially neuro-ectodermal. Martin, et al[12] try to reconcile these views by assuming that certain of these tumors arise from the ganglion of Loci, a small organ situated at the anterior part of the olfactory placode and of placodial origin, which gives origin to ganglion cells and nerve filaments connected to the brain by pathways as yet ill-defined; Loci's ganglion belonging to Nerve 0 (terminalis). Thus these tumors as well as the ganglioneuroma belong at least to the endodermal placodial system.

Dr. Farber suggested to us the possibility of the origin of these tumors from Jacobson's organ. In discussing Berger and Coutard's article[14] M. Peyron also considered that their "esthesio-neurocytoma" was "susceptible of being traced to the organ of Jacobson" (p. 414). Recent correspondence with Maj. Gen. Raymond O. Dart revealed that in the Registry of the Army Medical Museum there was "one peculiar tumor of the floor of the nose which was considered to be neurogenetic or possibly a transitional cell carcinoma or even an aesthesioma (an olfactory nerve tumor)." This is interesting considering Farber's and Peyron's views.

It is worth noting that these intranasal neuroblastomas appeared in adults while several recent intranasal gliomas[2] were found in infants of less than one month; in two cases the tumor was discovered at birth and was visible in the right nostril as a polyp. The fact that the three tumors here described composed of neuroblasts occurred in adults, suggests Cohnheim's theory of cell rests and his concept of restricted unicentric origin and purely intrinsic growth. Willis (p. 106) however considers that this view is false and believes that "tumors arise from small or large fields of tissue and enlarge not only by cellular proliferation but also by progressive neoplastic conversion of tissue within those fields."

In two of Cuthbert's cases spinal fluid escaped from the center of the tumors during removal. In only one of those here reported (Case 3) was fluid obtained and this most likely was caused by tumor erosion of the anterior fossa and not from the tumor itself.

SUMMARY

Three cases of primary intranasal neuroblastoma are presented making a total of 17 described in the literature. Clinically they appear in adults as obstructing nasal polypi indistinguishable from the banal polyp but for a greater tendency to bleed when touched and

presenting a redder, firm appearance. They are benign but have a tendency to malignancy if primary removal is incomplete. Their origin is still obscure but prevailing opinion is that they are of ectodermal origin and, more precisely, arise from the olfactory membrane. More case reports and differential staining studies are necessary to confirm this theory.

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XIX

MODERN BACTERIOLOGY AS AN AID TO THE OTOLARYNGOLOGIST

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The modern development of chemotherapy and antibiotics has opened new fields to the bacteriologist. In the past, recognition of the infecting organism in cases of bacterial infection was of purely academic interest. Later the development of specific immune serum treatment made it important to identify the bacterial organism involved so that the proper antiserum might be administered as rapidly as possible. However, this type of specific serum therapy was strictly limited to a few types of infections and others had to be treated with supportive measures only, thus giving the natural resources of the body the opportunity of overcoming the infection as best they could.

With the development of the sulfonamides and antibiotics it became still more important to know what the infecting organism was. It is no longer enough to know whether one is dealing with a gram positive or gram negative type of infection; one must know the exact nature of the infecting organism and its sensitivity to the antibiotics.

The bacteriologist should play an important part in helping the otolaryngologist to diagnose and treat infections. Bacteriological studies should include smears, routine aerobic and anaerobic cultures and antibiotic sensitivities.

In infections of the upper respiratory tract the smear can be a guide as to the type of predominating organism. One can quickly determine whether the organisms are predominantly gram-positive or gram-negative. In cases of severe infections, such as acute epiglottitis and laryngo-tracheo-bronchitis, it is important to determine the nature of the infecting organism without delay. If the infection is gram negative one can set up a quick Alexander preparation by mixing a loopful of secretion from the patient, a loopful of methylene blue and a loopful of Hemophilus Influenza typing serum, type B. The preparation is examined under oil in twenty minutes for the so-

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Read before the 36th Clinical Congress of the American College of Surgeons.

called "quellung" reaction. If this is positive the infecting organism is known and specific treatment can be begun immediately.

In cases of membranous tonsillitis or pharyngitis smears and cultures should be made. Information may be obtained by teasing away a piece of the membrane and making at least three smears. One is stained by Gram stain, one by Fontana stain and one with methylene blue. The Gram stain gives an idea of the predominating type of bacterial flora, the Fontana stain demonstrates spirochetes and fusiform bacilli and the methylene blue shows the presence of diphtheria bacilli and the spores and mycelia of the common fungi such as monilia and aspergilli.

In intracranial complications following an ear or a nasal infection almost any of the common bacteria may be the cause. Successful treatment may depend upon the speed with which adequate chemotherapy is combined with required surgical procedures. The bacteriologist should make immediate smears of all purulent material and spinal fluid in these cases. If organisms of the hemophilus or pneumococcus groups are suspected, "quellung" preparations with specific antisera should be set up immediately, and aerobic and anaerobic cultures made as soon as possible. We stress anaerobic cultures because, in our experience, many of the common pathogens such as pneumococci and beta hemolytic streptococci can be isolated much more readily by anaerobic culture. In aerobic cultures they may be overgrown by secondary bacteria such as E. coli and staphylococci. Organisms of the bacteroides and streptococcus faecalis groups are strictly anaerobic and may be missed completely unless anaerobic cultures are done. As soon as good growth has been obtained, antibiotic sensitivities should be determined by the bacteriologist using every antibiotic which may conceivably be effective.

Even in the treatment of low-grade indolent chronic infections such as external otitis, bacteriological studies and the proper selection of antibiotic may save the patient annoyance and money. It has been our experience lately, that many cases of external otitis which were formerly considered to be caused by a fungus are really due to bacterial organisms. By far the most common bacteria causing this type of infection are those of the staphylococcus, colon-aerogenes, and pseudomonas groups. Once the bacteriology is known, the proper drug can be used.

Through *in vitro* studies, the bacteriologist can often guide the physician as to the most effective drug to use. Recently we have seen two patients with chronic ulcers clinically resembling the chronic phagedenic type described by Meleney. Both patients had been treat-

ed with crystacillin but the ulcer continued to spread. Aerobic and anaerobic cultures were taken from several areas and from under the undermined edges. In each case the only organism isolated was a coagulase positive, hemolytic staphylococcus aureus. Antibiotic sensitivity tests were made and in each case the organism was found to be penicillin resistant but sensitive to both bacitracin and aureomycin. Bacitracin was administered locally and aureomycin was given orally. On this regime extension of the ulcer immediately ceased. In a few days it began to look cleaner and gradual healing took place.

The bacteriologist should be constantly on the alert to the possibility that the use of antibiotics disturbs the normal antibiotic relationship which exists between the different bacteria in vivo. For example, prolonged treatment with penicillin often results in a shift from normally gram positive to a gram negative flora. Occasionally this may prove very serious. Reports of E. coli bacteremia following treatment with penicillin and an abundance of E. coli in the throat. The change of flora in infants with meningitis from h. influenza to staphylococcus while on streptomycin has also been observed. We are now seeing in the nasopharynx bacteria which are usually isolating from the intestinal tract. Chief among these are bacteria of the colon-aerogenes and b. proteus groups. The use of antibiotics very often retards the growth of a culture so that it may take as long as five days for the organism to grow. Chief among these organisms whose growth is markedly slowed down is the diphtheria bacillus.

Often, after a patient with diphtheria has been given penicillin, it is almost impossible to demonstrate the bacilli by smear. In one case after crystacyllin was given it was necessary to make fifteen smears before finding the bacilli. In these cases, the bacteriologist must stress to the physician that he must be guided by the clinical picture and specific antiserum must be given as soon as possible in spite of negative smears.

The otolaryngologist is often called upon to see patients who have developed complications as the result of local antibiotic treatment. Now that antibiotic troches can be bought without a prescription they have become a popular form of self-medication. In addition, many general practitioners and dentists prescribe them. The most common form of lesion following this type of therapy is a severe stomatitis and an inflammation of all the mucosa of the throat and pharynx. Many of these patients develop severe fungus infections of the areas involved. The most common fungi isolated are those of the monilia group. The bacteriologist must rule out

this sensitivity. Withdrawal of the drug is usually sufficient for cure, and improvement starts shortly unless there is a fungus infection present, in which case proper fungicidal therapy should also be given.

With the numerous antibiotics and chemotherapeutic agents in use one must not lose sight of the immunological aspect of disease. There are still many diseases which cannot be controlled by the drugs now available and one must still resort to the biologicals. In ophthalmology and otolaryngology the most common pathogen encountered in chronic recurring infections is the coagulase positive hemolytic staphylococcus aureus.

This is not surprising since many workers have shown that approximately 50% of healthy people harbor it in the anterior nares. When the defense barriers of the body are let down these ever present bacteria cause infection. Antibiotics will usually take care of the acute phase of the disease but will do nothing to prevent further attacks. Even before chemotherapy when patients recovered from severe staphylococcic infections with bacteremia, it was not unusual for them to develop no circulating antibodies. Now with the antibiotics, the natural defense mechanism of the body has even less chance to develop them. The use of vaccine or toxoid in these patients has long been a source of controversy. Dr. Champ Lyons,[1] formerly of the Department of Surgery of the Harvard Medical School, demonstrated that young actively growing cultures of staphylococci are encapsulated and that the capsular substance is the antigenic factor important in preparing vaccines. He found also that some of the effective commercially prepared toxoid preparations had this capsular antigen. On this theory we have, since 1944, been preparing young culture vaccine of staphylococci. Enough here to say that the clinical results are more than encouraging and will be reported later.

I feel that the bacteriologist working closely with the clinician can help him to better treat his infectious cases. The bacteriologist should follow the clinical course of the patient with repeated cultures and sensitivity determinations.

He should be constantly on the alert for new antibiotics, for reports of untoward reactions as a result of antibiotic treatment and should try to keep the busy physician up to date on all these developments.

SUMMARY

With the large number of antibiotic drugs now available an accurate and rapid diagnosis of the infecting organism and its sensi-

tivity to the various antibiotic drugs is essential to the proper treatment of the patient. By using smears, aerobic and anaerobic cultures and immunological procedures the nature of the organism may be determined within twenty-four hours.

By determining antibiotic sensitivities with every drug which might conceivably be used to treat the case in question the bacteriologist can take the guesswork out of the treatment. By following the clinical progress with repeated cultures and sensitivity determinations he indicates to the physician the success or failure of his treatment by scientific proof.

The bacteriologist can further aid the specialist by keeping him informed of the daily advances in the field of antibiotics, by being on the lookout for the many complications which can occur as a result of antibiotic treatment and by evaluating laboratory findings in the light of the treatment used.

The bacteriologist should not lose sight of the fact that antibiotic treatment is not always able to control infections, especially those of a chronic or toxic nature. In cases of this type, one must still resort to the biologicals.

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XX

A BROKEN NEEDLE IN THE TONSIL FOSSA

A CASE REPORT

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The patient was a young adult in good health. Because of his apprehensiveness the operation was performed under general anesthesia. There was rather profuse bleeding from the tonsil beds. A Davis tonsil needle was grasped with a straight needle holder and the needle inserted into the upper part of the right fossa. Just as the needle was fully embedded (except for the end held by the holder), it broke. Only the eye and suture came out with the needle holder.

Removal at once was of course attempted, but each time the fossa was explored, profuse bleeding occurred, and failure resulted. The patient was told of the accident and an x-ray was taken, showing the needle just lateral to the superior third of the fossa. There was at first an uneventful recovery.

Some weeks later, however, the patient reported vague pains in his throat, on the side of the accident. Whether these were real or imagined could not of course be determined, but because of these and of our desire to remove the needle, another exploration was attempted. The usual fluoroscope with or without the hand screen was unsatisfactory. Therefore a biplane fluoroscope, operated of course by a competent radiologist, was used. A Burman metal detector was also used. This is an electrical instrument, shaped like a pencil, which emits a buzzing sound which increases as the instrument approaches the object. A non-metalic mought-gag is preferable when using this instrument.

Under ether anesthesia, a small incision was made just lateral to the upper part of the tonsil fossa. This was deepened by blunt dissection, great care being exercised not to injure any of the surrounding structures. A mosquito hemostat was introduced and attempts were made to grasp the needle, with the aid of the fluoroscope and Burman detector. It was certain that we were close to, if not at times actually touching it, but at no time were we able to grasp and remove it. The procedure was finally abandoned after almost two hours' effort.

This time, at the family's request, the patient was told that the removal had been successful. (Note: The legal aspects should be borne in mind). Convalescence was uneventful, and there have been no symptoms to date (4 years later).

The cause of this accident may have been one of the following: the needle holder may have been too heavy for the needle and may have exerted too much force upon it, the needle was probably grasped at the weakest point, i.e. the juncture of the shaft and the eye, or the needle may have been defective.

To avoid such an accident other means of hemostasis may be employed, such as: a needle on a handle with the eye in the tip, a purse string ligature, a Shuster or other automatic type of needle. Many however, prefer to use a plain needle and needle holder regardless of the dangers. If so, the following precautions should be exercised: a very light needle holder should be used; the needle should be grasped below and not at the junction of the eye and the shaft, and the needle's strength should be tested with the fingers before using it.

The needle should be of heavy caliber, three fourths of an inch long, quarter circle curve with a strong eye large enough to carry up to number one catgut without straining the capacity of the eye. It is desirable that to prevent rotating, the needle have a square shank with the distal quarter inch forming a point with a round shank.

The needle holder may be of any type that enables the operator to visualize the field, permits insertion of the needle at its natural curve and does not grip the needle with excessive force over too great an extent of its curved surface.

Dr. Davis devised a needle holder that is most satisfactory. It is angulated like the nasal alligator grasping forceps with short jaws set at an angle to the shaft like a small foot. Only the upper jaw of this foot is moveable. There is no lock such as the hemostat catch, thus eliminating the chance of too great pressure being applied to the needle. This is one of its most commendable safety features.

The Davis technique for inserting the suture ligature consists of using a long, slightly curved artery forceps to seize the bleeding vessel with as little of the surrounding tissue as possible. The threaded needle is grasped well away from its eye at a right or obtuse angle to the jaw of the needle holder. The needle is inserted from medial to lateral beneath the vessel, penetrating and including the smallest possible amount of tissue. The needle is inserted with no more than a

quarter circle motion, in order to avoid placing excessive leverage or torsion on the needle, until the point emerges on the lateral side of the vessel. The needle remains in the grasp of the holder until the point is firmly seized with a nasal alligator grasping forceps and withdrawn from the throat. The needle is then unthreaded and the suture tied.

Complications occurred in 12% of the cases compiled by Weiss.[1] They included: fracture of the hyoid bone during attempted removal, persistent neuralgic pain over the course of the glossopharyngeal nerve, parapharyngeal space infection, and pain on swallowing. As was mentioned above, this patient has had no symptoms so far, a matter of over four years.

Some interesting points were revealed when this case was presented at a meeting of the Section on Otolaryngology of the College of Physicians:

Breaking a needle in the tonsil fossa is evidently not too uncommon an accident. Of some 50 members present, there were 14 who had had that experience, several had had it more than once. Most of these needles were unrecovered. More than half the lost needles were, however, those used for injecting local anesthesia, rather than the kind used for suturing. Several of the former type were removed by the use of the electromagnet. Dr. E. P. Longaker has modified the usual electromagnet used for removing metallic objects from the eye. He has made the tip longer and thinner so as to enable it to be better placed inside the oral cavity.

Only one complication was reported. This was a death from pulmonary infection, due to over-long anesthesia during an attempted removal. There was mention of one needle that had migrated to several places in the neck, but without symptoms.

SUMMARY

A case of an unrecovered needle in the tonsil fossa is reported. Methods of prevention of such an accident, means recovery of the needles, and possible complications are discussed.

1 Summit St.

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Clinical Notes

XXI

CARCINOMA OCCURRING IN AN ANTRO-ALVEOLAR FISTULA

CASE REPORT

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AND

IRVING I. GOODOF, M.D.

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While the formation of an antro-alveolar fistula secondary to carcinoma of the antrum is fairly common, especially when the neoplasm originates in the lower portion of the sinus, the occurrence of malignant changes in an already existing fistula is an unusual finding and prompts the following case report:

W. K., white male, age 41, was referred by his family physician because of pain and a tender mass on the alveolar process of the maxilla of one month's duration. This had been followed by swelling just below the mandible on that side. All teeth had been extracted twenty years before at which time the right antrum had been entered inadvertently. An antro-alveolar fistula in the socket of the first molar tooth resulted. While there had been a constant discharge from this tract, the patient had made no attempt to have this corrected. Examination revealed an ulcerative, cauliflower-like tumor on the buccal aspect of the alveolar process, in the center of which was a fistulous tract to the antrum. There was a swollen indurated mass in the submaxillary triangle of the neck. Biopsy was reported as follows: "The gross specimen consists of several irregular, friable, gray-white bits of tissue showing no specific gross characteristics. Microscopically the specimen shows only slight irregularity of the surface epithelium, which is stratified squamous in type. The underlying tissue is replaced by roughly spherical masses of anaplastic epithelial cells, some of which appear to arise from the basal layers of the surface epithelium. Although many of

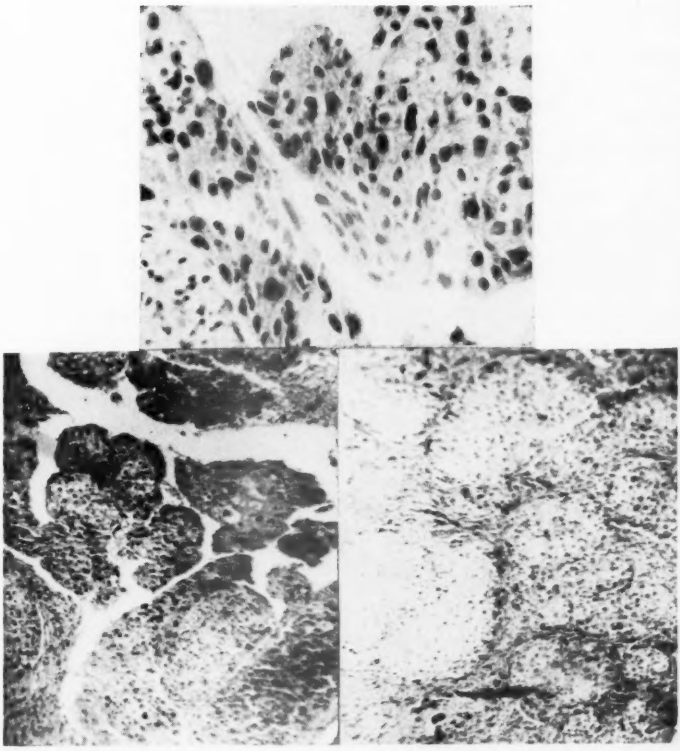

Fig. 1.—Photomicrographs of tumor from antro-alveolar fistula and antrum. Lower photomicrographs show the large, irregular pale cells originally suggestive of ameloblastoma. Upper photograph is more characteristic of the picture seen in most of the specimens removed after the original biopsy. The cells are smaller, more dense, and typical of epidermoid carcinoma.

these nests are composed of closely packed polygonal cells consistent with epidermoid carcinoma, some areas show large cells with clear cytoplasm, suggestive of ameloblastoma. The overall architecture, however, is distinctly squamous in type." (I. I. G.)

Diagnosis: "Epidermoid carcinoma, Grade III."

Roentgenogram showed the right antrum completely opaque but with no apparent loss of bony walls. The Hinton test was positive and antiluetic penicillin therapy was instituted.

Operation: Anesthesia: Avertin, plus procain block. The antrum was found completely filled with the tumor mass which had protruded through the anterior-inferior wall in the region of the alveolar fistula and the adjacent canine fossa. The posterior wall was eroded exposing the pterygoid fossa. The remaining bony walls of the antrum were intact. The cutting current was used to expose the canine fossa and demarcate the protruding tumor, following which the tumor mass was destroyed by extensive electro-coagulation. Ninety milligrams of radium was implanted in the operative cavity and left to deliver a dosage of 3,000 millicurie hours. Material removed at this time was also reported as epidermoid carcinoma, Grade III. Exploration of the neck revealed a mass of partially broken-down neoplastic tissue, apparently inoperable. Histopathologic examination of this material was also reported as epidermoid carcinoma, Grade III.

The patient was given intensive external roentgen therapy to both sides of the neck. There was a rather marked radiation reaction involving the mouth, tongue and palate. The condition of the antrum appeared satisfactory and he seemed considerably improved for about three months. Later, however, recurrence developed in the antrum together with marked tumefaction of the neck. He gradually failed, became irrational and expired eight months after operation. Postmortem examination revealed a broken-down mass of neoplastic tissue in the right side of the neck together with metastases to the nodes in the left side. There was no evidence of intracranial extension, but the process had invaded the pterygoid fossa, palate and base of the tongue.

Discussion: Here we were dealing with a typical, rapidly growing carcinoma of the antrum with marked cervical metastases. When first seen, the condition seemed too far advanced to make extensive neck surgery feasible. The grade of the tumor suggested the possibility of some response to irradiation, but as is usual with such metastases, this proved futile. The hopelessness of this situation was further emphasized by the recurrence in the antrum after what ap-

peared for a time to have been a satisfactory response to irradiation. The etiology is interesting. While it is not unusual for malignant change to occur in a case of chronic sinusitis, the authors are not aware of any similar changes taking place in an antro-alveolar fistula. Actually the distinction is rather academic, as the long-standing fistula resulted in a chronic sinusitis which later underwent neoplastic changes. That this must have been a comparatively recent development is suggested by the rapidity of the tumor growth. The possibility, however, of actual origin of the tumor within the fistulous tract itself, must be given consideration. The existence of a chronic inflammatory process such as would be found in an antro-alveolar fistula may certainly have played a contributing part in the development of the malignant changes which occurred in this patient. This case emphasizes the importance of early correction of an antro-alveolar fistula. The usual sequelae of persistent oral drainage and the symptoms of a chronic purulent sinusitis are, in the main, more of an annoyance than a danger. It is well to keep in mind that a persistent antro-alveolar fistula may lead to conditions of lethal import and that correction of the condition as early as possible is highly desirable.

THAYER HOSPITAL.

XXII

SCHWANNOMA OF THE TRACHEOBRONCHIAL TREE

A CASE REPORT

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AND

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Benign intrathoracic tumors are relatively rare. Compared with malignant neoplasms they are considerably less important in point of view of number, but are relatively more important because of their operability and curability. It is possible to have any type of tumor originate within the thorax because histologically each of the three primary germinal layers is represented in the embryologic development of the chest and its contents.[1] With the gradually increasing use of bronchoscopy in cases of various pulmonary lesions, interest in intrabronchial tumors has greatly increased, and this is the chief reason why these tumors now appear to be steadily increasing. In 1939, Lindgren[2] reviewed the world literature on benign bronchial polyps and uncovered a total of 181 cases. They were reported as follows: Adenomas 133, mucous polyps 17, fibromas 12, chondromas 9, lipomas 5, papillomas 3, lymphoma 1, and mixed tumor 1. Since bronchoscopy has made tremendous strides in the past 11 years, the number of intrabronchial tumors diagnosed would be greatly increased if such a survey were made today.

The following case is that of a schwannoma, polypoid in character, attached at the orifice of the left main stem bronchus and causing partial obstruction of that bronchus.

CASE REPORT

The patient was a 28-year old white male who entered the hospital on October 11, 1949, complaining of chills, fever, nasal con-

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gestion, general malaise, and a cough productive of a large amount of purulent green exudate. These symptoms had been present for the previous four days. Past history revealed that the patient had been having similar episodes every spring and fall since 1945. During the initial attack in the spring of 1945, the patient also had a cough productive of a blood-tinged sputum; however, hemoptysis had not recurred since 1945. The previous illnesses had been diagnosed as lobar pneumonia, and all episodes responded readily to chemotherapy. Between attacks the patient felt well. There was no history of allergy or bronchial asthma.

Physical examination on admission revealed a well developed, well nourished white male, age 28, who had a temperature of 99.2° F. but otherwise did not appear especially ill. Positive physical findings were as follows: The nasal and pharyngeal mucous membranes were congested and hyperemic; the tonsils were moderately hypertrophied; and the chest exhibited diminished breath sounds and expiratory wheezes over the posterior and lateral inferior portion of the left chest.

Laboratory Examinations: WBC on admission was 14,700 with 62% segmented forms, 5% stabs, 2% lymphs, and 12% monocytes. Sedimentation rate was 36 mm per hour. Hemoglobin was 13.5 gm. Serology was negative. Admission chest x-ray showed an indefinite increased density in the left base.

The patient's symptoms responded readily to chemotherapy, and he was bronchoscoped after the pneumonic process had subsided. The trachea appeared essentially normal except for the presence of a moderate amount of purulent appearing exudate. When the carina was approached, a tumor mass was seen which was irregular in outline. It appeared on the posterolateral wall of the left main stem bronchus and was about 12 mm in diameter. When touched, this mass did not bleed easily. The right main stem bronchus was essentially normal in appearance. The bronchoscope was advanced past the tumor into the left main stem bronchus. The mucous membrane appeared hyperemic, and purulent appearing exudate was visualized coming from the left lower and left upper lobes. A biopsy was taken. A diagnosis of schwannoma was made. Bronchograms were then done (Fig. 1), and the tumor mass seen on bronchoscopy was demonstrated with Bucky films and described as a filling defect measuring 2 cm in its greatest diameter and approximately 1 cm at its base. This mass apparently extended from the left posterolateral wall of the trachea just above the junction of the trachea and the left main bronchus. Partial obstruction of the left main bronchus was noted on expiratory and inspiratory views.

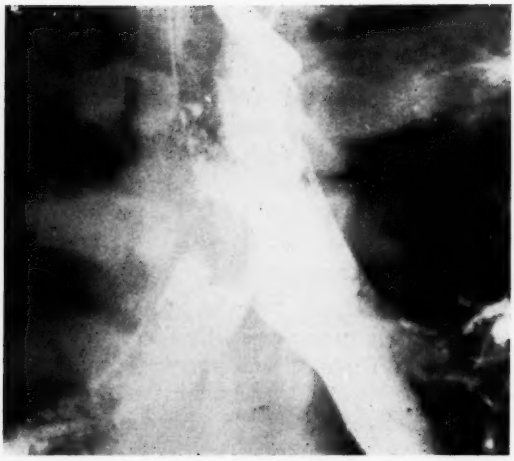

Fig. 1.—Bronchogram shows a filling defect apparently projecting from left postero-lateral wall of trachea just above junction of trachea and left main stem bronchus.

It was then decided to remove the schwannoma endoscopically in as many stages as were necessary. Two stages were required to remove it completely, and the base was cauterized with 20% silver nitrate. Further microscopic sections confirmed the original diagnosis. The patient's course in the hospital was uneventful, and he was discharged with instructions to return in six weeks for a follow-up examination.

Six weeks' follow-up revealed the patient to be completely asymptomatic and he had gone back to work. He was bronchoscoped again, and the tracheobronchial tree appeared normal except for a small stellate scar at the junction of the trachea and left main bronchus where the tumor was removed.

Discussion: The most common site of primary solitary neurogenic tumors in the thorax is the mediastinum. They are extremely rare in the lung. Numerous neurofibromas involving the lung, either primarily or by sarcomatous extension, are reported in patients afflicted with multiple congenital neurofibromatosis. In reviewing the literature of the past ten years one other case of solitary primary neurogenic tumor of the lung was found. This was a case of a neurinoma reported by Bartlett and Adams[3] in 1946, which was removed by total pneumonectomy. It was firmly attached to the left

main stem bronchus, but lay in the surrounding lung tissue and caused stenosis of the left main stem bronchus.

Stout[4] divides the benign growths which develop from nerve sheaths into two common varieties—the neurofibroma and the neurilemmoma. The neurilemmoma is known by a variety of names such as the neurinoma, perineurial fibroblastoma, schwannoma, peripheral glioma, or Schwanno-glioma. The distinguishing features of each are as follows:

The neurifibroma is a diffuse growth of Schwann sheath cells and fibrous tissue associated with von Recklinghausen's disease either occurring at the end of the nerves in the skin or producing thickening and tortuosity of nerve trunks (plexiform neurofibroma) or forming elephantoid enlargement of the skin, bones, or intestines (elephantiasis neuromatosa). The neurofibroma may occasionally become malignant.

The neurilemmoma or schwannoma, on the other hand, is always an encapsulated tumor found within or attached to the nerve sheath and almost always solitary. It is only occasionally associated with von Recklinghausen's disease. It has distinct histopathologic features which distinguish it from diffuse neurofibroma, and it is always benign as far as is known.

By far the most common benign intrabronchial tumor is the adenoma,[5] but the symptoms usually produced by any intrabronchial benign polypoid tumor are not due to the tumor itself but to the secondary lung changes caused by the obstruction. For this reason they will inevtiably be fatal unless removed. Since the symptoms from intrabronchial masses are mostly the result of secondary lung complications, the tumor may be asymptomatic for months or years until it has grown large enough to partially or completely obstruct the bronchial lumen. At the most it may cause a slight cough, dyspnea, or hemoptysis, and for this reason tuberculosis frequently is first suspected. The lung complications of atelectasis, recurrent pneumonia, bronchiectasis, or dry or exudative pleuritis are most common. Empyema is rare and is observed mostly in advanced stages. Hemoptysis occurs periodically and begins and ends abruptly.

In diagnosing intrabronchial neoplasms the most dependable and surest method is by direct visualization of the tracheobronchial tree through the bronchoscope. X-ray examination can only reveal some of the lung complications such as atelectasis, pleural exudate, pneumonia. Bronchograms with lipiodol may indirectly indicate a stenosing tumor.

The removal of benign tumors is a very satisfactory procedure both from the standpoint of the patient and the surgeon since a permanent cure usually follows a successful operation. The characteristics of benign neoplasms, such as encapsulation and lack of invasion and metastasis, permit complete surgical removal. The treatment of such benign intrabronchial tumors is local excision. Fortunately, in this case it was possible to completely remove the tumor through the bronchoscope. In patients in whom the neoplasm is not accessible to the bronchoscope or is too large for resection through the bronchoscope, lobectomy or even pneumonectomy is indicated. Even in those cases in which it is possible to remove the neoplasm through the bronchoscope, a recurrence of the lesion may necessitate further resection or more radical pulmonary surgery. The method of treatment of all benign intrabronchial masses depends on their size, location, disposition, radiosensitivity, and on the severity of the secondary pulmonary complications. Such patients must be followed for months and years so that further treatment may be carried out promptly if the tumor recurs.

VETERANS ADMINISTRATION CENTER.

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XXIII

GASTROENTEROSTOMY A CONTRAINDICATION TO THE USE OF A SWALLOWED SILK THREAD

BURNETT SCHAFF, M.D.

AND

M. H. TODD, M.D.

CORAL GABLES, FLA.

It is a common procedure to have a silk string swallowed as a guide for esophageal dilatations. The complications of dilatation are usually ascribed to the passage of the bougies or bags and it appears to be assumed that the swallowing of the silk guide is free of complications. However, this is not true if a gastroenterostomy or enteroenterostomy is present.

One of our patients undergoing dilatations for an esophageal stricture and wearing a swallowed silk thread, was operated on for a "bleeding anastomotic ulcer." At operation the stomach was opened and the silk thread was found to have looped itself through the pylorus into the gastroenterostomy stoma and then back around itself. The loop passed through the ulcer crater. Vinson in 1931 reported that this had also occurred in his practice, but felt that it gave rise to no difficulties. Hubbard and Levine reported two cases in which the use of a silk guide in the presence of an esophagojejunostomy and enterostomy led to difficulties. The thread at autopsy in both cases was found wound around the loop of jejunum enclosed between the esophagojejunostomy and jejunostomy. Erosion of the underlying vessels in one of these cases caused a fatal hemorrage.

REPORT OF A CASE

A 41 year old negro was admitted to the hospital on August 8, 1949 for the treatment of an esophageal stricture. A gastroenterostomy had been performed elsewhere in 1941 for hematemesis, pre-

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

sumably due to a peptic ulcer. Later, an esophageal stricture developed that was thought to have been caused by the Levine tube introduced into the stomach postoperatively for suction. Roentgenographic and esophageal studies, including biopsy, revealed an ulcerated and stenosed area 1 cm in diameter, about 5 cm above the diaphragm. A silk string was swallowed November 5, 1949, and subsequently bougies were passed over this string at weekly intervals. Severe attacks of hematemesis occurred on December 15, 1949, and January 28, 1950, and for that reason an exploratory laparotomy was done on February 13, 1950. A posterior gastroenterostomy with a stomal ulcer was found. The stomach was opened to explore the site of anastomosis and at this time several matted strands of silk were found. Attempts to remove them were unsuccessful. Further examination revealed that the string had passed through the pylorus into the jejunum and back through the anastomotic stoma into the stomach where it tangled about itself. The loop passed over the ulcer crater. The thread was cut in sections and easily removed. The effect on the ulcer of traction on this string during the dilatations can only be conjectured.

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XXIV

A CASE OF RHINOSPORIDIOSIS

ROBERT G. BOLES, M.D.

AND

SYDNER D. MAIDEN, M.D.

MEMPHIS, TENN.

REPORT OF A CASE

L. B., a twenty-five year old white male, farmer, was admitted to Kennedy Hospital for a tonsillectomy on June 27, 1950. During the course of his examination the patient gave a history of having had mild intermittent episodes of bleeding from the right naris over a period of three or four years. The bleeding would occur approximately every three weeks, associated with a slight increase in nasal congestion.

The patient has never been out of the United States. He states that the only time he has ever been away from home was while serving in the Navy about two years. He received his basic training at Bainbridge, Maryland, and spent twenty-two months at Norfolk, Virginia where he worked in an ammunition depot and drove a truck. The past three years have been spent on a farm raising vegetables, corn and cotton. The usual farm animals were present.

Examination of the nose revealed a mild septal deviation to the left with a spur inferiorly on the right. The spur was in contact with the inferior turbinate which appeared hypertrophied and was covered with dry mucus. When the mucus was removed a granular polypoid tip was seen on the inferior turbinate which bled easily. The remainder of the nasal mucosa was normal in appearance. A biopsy and smears were taken. Both smear and biopsy were reported as rhinosporidiosis (Figs. 1 and 2).

The remainder of history and examination were noncontributory. There was a small tumor on the left side of his external nose which was removed and reported as a sebaceous cyst.

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

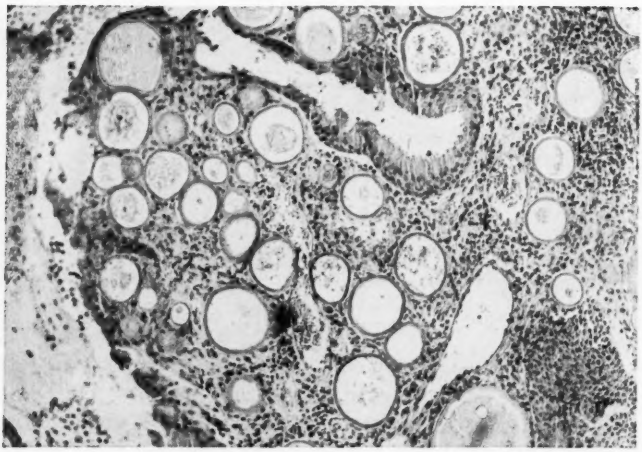

Fig. 1.—Rhinosporidiosis of nasal mucosa showing polypus containing numerous sporangia (H & E x 100).

The treatment consisted of surgical removal of the diseased portion of the anterior tip of the right inferior turbinate followed by electrical coagulation.

Laboratory Report: The specimen consisted of a tan rubbery piece of tissue which cut easily revealing a homogeneous tan cut surface. Microscopically the section consisted of fragments of granulation tissue covered partially by pseudostratified ciliated columnar epithelium which in many areas shows squamous metaplasia. The entire section is filled with numerous sporangia which vary from approximately 30 to 300 microns in diameter. These have a thick refractile hyaline capsule and the largest ones are filled with spores. The spores vary from 1 to 10 microns in diameter. Some of the larger sporangia are filled with mature spores which are breaking through the capsule into the surrounding tissue. The tissue shows chronic inflammation and occasional small collections of acute inflammatory cells. The organisms are typical of Rhinosporidium seeberi.

DISCUSSION

Rhinosporidiosis, although commonly called a tropical disease, has a wide geographical distribution, cases having been reported from India, Argentina, United States, North Africa, and Palestine. Young males are the most frequent victims. Only four of the 53 cases re-

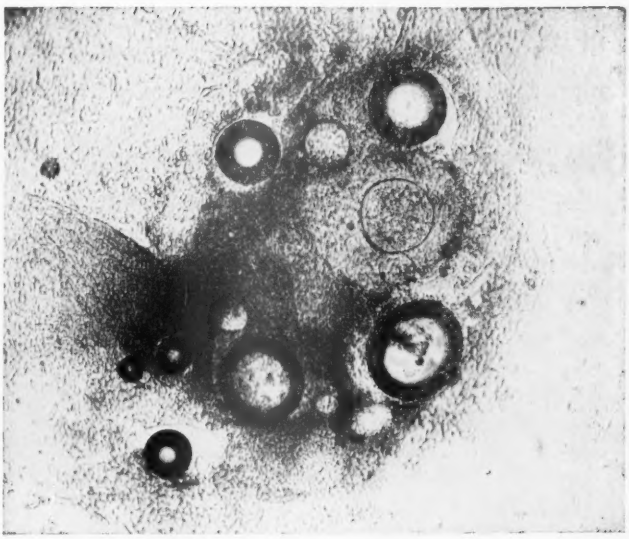

Fig. 2.—Sporangia seen on nasal smear.

ported by Ruchman[1] in August, 1939, were in females. Of these 53 patients, 40 had lesions in the nose, other sites being the conjunctiva, the ear, the pharynx, the larynx, and the penis.

It is of historical interest that the first case of Rhinosporidium seeberi reported in the United States was in a 20 year old Tennessee farmer described by Wright in 1907, with a lesion in the right naris involving the septum and inferior turbinate.

There have been 18 cases reported in the United States, twelve cases occurring in the nose and six which were conjunctival in origin.

The characteristic finding is a bleeding polyp in the anterior part of the nose. A severe coryza usually described as preceding and accompanying the formation of the polyp was not present in this case. Ashworth reports finding the characteristic organism in the mucopurulent discharge. This was found to be present on smear of nasal secretions.

The disease is produced by Rhinosporidium seeberi, a yeast or phycomycete, which is a round or oval cell containing clear, vacuolated protoplasm enclosed by a well-defined chitin with maturation of the spores. The sporangium enlarges until the thin film in one

area ruptures and the spores are disseminated into the lymphatics, and from there into the surrounding connecting spaces to develop to the trophic stage, thus completing the development cycle.

The present patient is a white male who developed rhinosporidiosis in the United States.

VETERANS ADMINISTRATION.

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XXV

TRAUMATIC HEMATOMA OF THE LARYNX

REPORT OF A CASE

LAWSON G. COX, M.D.

AND

ERNEST J. VAN EYCKEN, LT. COL. M.C.

WEST POINT, N. Y.

The reason for the relatively small number of injuries to the larynx is probably its protected situation, i.e. the protection offered by the chin, its lack of ossification in early adult life, and its immense mobility[1], in other words its ability to "roll with the punch."

A thorough search of the literature did not reveal any publications on traumatic hematoma of the larynx in the English language, and only few in a foreign one.[6] Therefore it seems worth while to report a case of injury to the larynx, the only objective finding of which was a hematoma of this organ.

REPORT OF A CASE

An 18 year old white male was brought to the hospital by ambulance on October 18, 1950. He stated that he had received a severe blow to the neck while playing football, the exact nature of which was not known. He was stunned momentarily but regained all his faculties after a few moments. However, upon trying to speak he noticed that he was extremely hoarse. In addition, he began experiencing difficulty and pain on swallowing, pain on phonation, and very slight dyspnea. No hemoptysis was noted. Other history was irrelevant.

Physical examination was essentially negative except for the following: there was considerable tenderness over the right side of the thyroid cartilage. This cartilage appeared intact when examined by palpation; crepitation could be elicited; no displacement or fragmentation could be felt. There was no change of configuration of

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From the ENT Department of U. S. Army Hospital, U. S. Military Academy, West Point, N. Y., Chief: Lt. Col. E. J. Van Eycken, M.C. The opinions expressed herein are those of the authors and should not be considered as the official policy of the Surgeon General.

the neck, especially no flattening of the laryngeal prominence. Indirect laryngoscopy revealed considerable edematous swelling of the right aryepiglottic fold so that the right vocal cord could not be seen. The part of this swelling over the right arytenoid region was hemorrhagic. Motion of the left vocal cord appeared normal, though its posterior half was obscured by the aforementioned swelling when the cord was in complete adduction.

No bloody sputum nor emphysema were noticed. X-ray examination on admission was negative for fracture and also when repeated after seven days. This was done, as X-rays for laryngeal fractures are sometimes positive only after a few days.

However, x-rays taken on October 25, revealed considerable swelling in the right side of the larynx both above and below the true vocal cords. This swelling occupied the right ventricle which was completely obscured. There appeared to be no appreciable swelling on the left side. Laboratory findings were normal.

Treatment consisted of complete voice rest, ice collar to the neck, penicillin parenterally, adrenalin spray, and liquid diet. On the fourth day the swelling had become diminished in size and a submucosal hematoma was noted filling the right ventricle. For the first time a hematoma could be seen below the right vocal cord, and a small area of ecchymosis was noted below the left one. The motion of both vocal cords now appeared normal though the right could not yet be completely seen when in abduction. By the end of the first week the patient was able to tolerate a soft diet; the hoarseness had improved somewhat. Absorption of the hematoma proceded without complications, and on the seventeenth day he was able to be returned to full duty with a normal larynx and without any symptoms.

COMMENT

Our first impression was that this patient might have sustained a fracture of the larynx. According to Kernan and Cracovaner[2] the symptoms of a fractured larynx are pain over the larynx, tenderness, swelling, usually hoarseness or aphonia, pain on swallowing; frequently difficulty in breathing due to edema, either immediately or soon after injury; shock at the time of the accident, and sometimes bleeding. Gardner[3] mentioned that in laryngeal fractures the pain is usually worse on phonation, that the hemoptysis is a common observation, and that crepitation can usually be elicited but should not be taken as a positive sign of fracture; nor should its absence rule it out.

All the above mentioned symptoms were present except bleeding, external swelling and disfiguration of the larynx. The crepita-

tion which was present was in our opinion produced by the normal larynx gliding over the surface of the cervical vertebrae. Mullen[4] warned not to mistake this sensation for true crepitus, caused by fracture of the larynx. We did not feel that a diagnosis of fracture of the larynx was justified because of the absence of these important symptoms, and because the patient was not in too serious a condition. In retrospect we feel that the patient would not have recovered as rapidly had a fracture been present.

All the symptoms and findings can be explained on the basis of a laryngeal contusion alone. The shock the patient suffered immediately after the injury was in our opinion caused by concussion of the larynx, for during the accident the larynx was undoubtedly moved and pressed on the nerves or vessels of the neck or both. It is known that slight pressure on the sympathetic or the parasympathetic nerves, of which the larynx has an ample supply, may result in sudden unconsciousness or even death, and that a compression, even of short duration, of the big vessels in the neck or of the carotid sinus might have the same consequences. It is a fact that a contusion of the larynx may cause a laryngeal edema,[5] also a hematoma without fracture of the underlying cartilage. The reason that this patient did not suffer a laryngeal fracture in spite of the severe blow to his neck is probably that at his age the thyroid cartilage was not ossified.

U. S. Army Hospital.

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New Instrument

XXVI

BRONCHOSCOPIC CANNULA FOR INTRODUCTION OF IODIZED OIL INTO TRACHEO-BRONCHIAL TREE OF CHILDREN

JAMES A. HARRILL, M.D.

WINSTON-SALEM, N. C.

Securing adequate filling with iodized oil in the tracheo-bronchial tree of infants and young children, in whom the intra-tracheal catheter method cannot be used, is often difficult. The cannula presented in figure 1, has often been of considerable help to me in the introduction of iodized oil through the bronchoscope.

The cannula may be made in various lengths from brass tubing of bronchoscopic light carrier caliber. A Luer-Lok attachment is fixed to one end of the tube.

After the tracheo-bronchial tree secretions have been aspirated, the bronchoscope is withdrawn to approximately 1 cm. above the carina, the lightcarrier is removed and the special cannula is introduced into the light carrier channel of the bronchoscope down to the distal end. The desired amount of oil is then delivered. The child may be tilted before injection to the right or left side, or both, as desired.

The cannula offers several advantages:

1. By utilizing the light carrier channel, the cannula does not encroach upon the bronchoscopic airway.

2. The distal end of the cannula cannot traumatize the tracheal or bronchial mucosa.

3. The oil is delivered at the distal end of the bronchoscope.

4. A large portion of the oil, if the injection is made slowly, will enter the side elected.

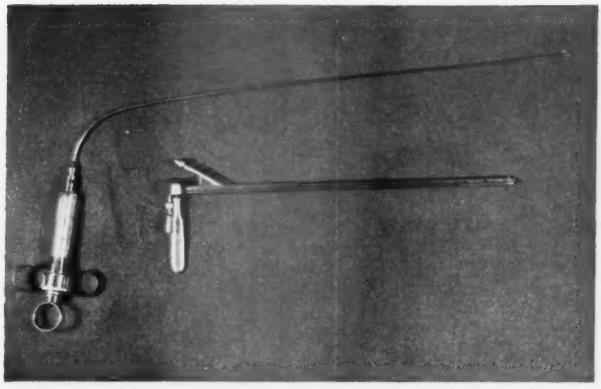


Fig. 1.—Bronchoscopic cannula for introduction of iodized oil into tracheobronchial tree of children.

5. The Luer-Lok arrangement gives secure attachment to the syringe.

Department of Otolaryngology and Broncho-Esophagoscopy, Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, N. C.

Society Proceedings

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, November 6, 1950

THE PRESIDENT, DR. SHERMAN L. SHAPIRO, IN THE CHAIR

Tracheotomy in Tetanus

EMANUEL HERZON

AND

EDWIN KILLIAN

SUMMARY

An historic resume of cases of tetanus requiring tracheotomy is presented together with reports of six cases. The various theories of pathogenesis are presented, followed by a discussion of the pathology and pathologic physiology. Treatment of tetanus as a respiratory problem is discussed.

Myxofibrosarcoma of the External Auditory Canal

HANS VON LEDEN

(Abstract of Case Report)

A 13 year old Negro was admitted to Cook County Hospital with a tumor of the right external auditory canal, and a complaint of diminished hearing. The past history indicated that two surgical excisions of the tumor and a course of roentgen therapy had failed to destroy the neoplasm.

The patient presented a light brown mass protruding from the right external auditory canal, resembling cauliflower in appearance. The neoplasm filled the canal completely and displaced the tragus and concha laterally. It was firmly attached to the anterior wall of the canal by a broad base. Hearing tests indicated a hearing loss of the conduction type on the involved side. Roentgenograms showed

normal aeration of the mastoid portions of both temporal bones. A biopsy from the protruding superficial portion of the tumor indicated a hyperkeratotic papilloma with embedded epithelial cysts and submucous collections of lymphocytes.

The entire tumor and a surrounding strip of apparently normal skin were excised, and the defect was covered by a thin split-thickness skin graft. Microscopic examinations of the excised tumor revealed large areas of fibromyxomatous tissue with the characteristic appearance of a well-differentiated myxofibrosarcoma.

The postoperative course was uneventful; the external auditory canal resumed normal proportions and hearing tests indicated restoration of the hearing to the normal level. The patient appeared free of any disease for a period of eight months. A recent examination, however, revealed recurrence of the tumor in the same area, with extension to the posterior wall of the external auditory canal.

Otogenous Intracranial Complications

JOHN ELSEN

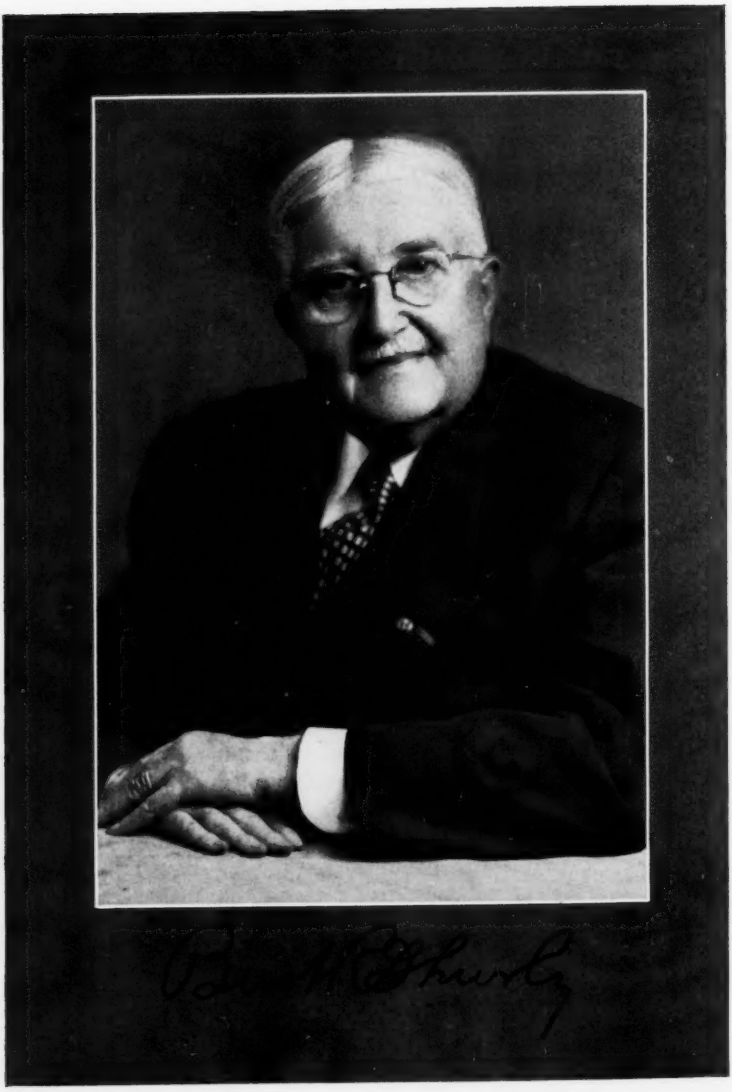
ELMER A. FRIEDMAN

AND

NORMAN LESHIN

(Abstract)

Four cases of intracranial complications from chronic ear infection are presented. Two cases of perisinus abscess and lateral sinus thrombophlebitis, one with fatal termination, one case of temporal lobe abscess, and one case of extradural abscess and purulent meningitis are reviewed, with comment on the handling of each case. The masking effects of sulfonamides and the antibiotics are discussed and demonstrated. In lateral sinus thrombosis and brain abscess the various methods of treatment are outlined. The use of intrathecal penicillin in cases of meningitis from ear infections is emphasized. Thorough surgical removal of the mastoid focus in infection and the intracranial complication is as important today as before the advent of the sulfonamides and the antibiotics.



BURT RUSSELL SHURLY, M.D.

1871-1950

With the passing of Dr. Burt Russell Shurly of Detroit, Michigan, we have lost a pioneer in otolaryngology, and an eminent civic leader.

When a thousand Detroiters from all fields of life tendered him a testimonial dinner in 1940, Journalist George W. Stark wrote that, "Dr. Shurly's career has touched so many phases of life that the banquet diagnosticians had to take it up piecemeal, operating in sections. A very gracious pattern emerged, which seemed to teach the assemblage that the Doctor's way of life has been something for us all to emulate."

Dr. Shurly was born July 4, 1871, at Chicago, Illinois, son of Col. Edmund R. P. Shurly of the United States Army. Like father, like son, young Burt attended public school in Chicago, Northwestern Military Academy and the University of Wisconsin. At the latter institution he was tennis champion, football manager and campus editor.

In 1892, on the advice of his uncle, Dr. Ernest L. Shurly of Detroit, Burt transferred his student activities to the Detroit College of Medicine, receiving his degree of M.D. in 1895. After a postgraduate course at the University of Vienna, he became associated with his uncle in the practice of otolaryngology and the treatment of tuberculosis. The Shurly Hospital, which developed from this association, operated in down-town Detroit from 1915 until 1947.

In the meantime, Dr. Shurly lectured at his medical Alma Mater, serving as dean for many years. In 1913, when the college, a stock corporation, became financially embarrassed, he bought it outright, reorganized the entire system and pioneered pre-medical training in the city's Junior College. This was the beginning of the present Wayne University College of Medicine.

Dr. Shurly's medical career was twice interrupted by war. As a volunteer he served as Assistant Surgeon in the Spanish-American War on one of the ships that helped destroy the Spanish fleet. In World War I, he organized and commanded Base Hospital No. 36, which was located at Vittel, France. For meritorious service there, Lt. Col. Shurly was awarded the Legion of Honor by the French Government.

Among his noted civic achievements was the founding of the Detroit Tuberculosis Society, which led to the establishment of the Detroit Tuberculosis Sanitorium, and the Leland Sanitorium at Ypsilanti. During the Doctor's twenty-three years as member of the city's Board of Education, with four terms as its president, his "genius for vision affected many areas."

Honored in the national medical field since the turn of the century, Dr. Shurly had served in various capacities; as President of the American Laryngological Association; Vice President of the American Board of Otolaryngology; President of the American Academy of Ophthalmology and Otolaryngology; President of the American Laryngological, Rhinological and Otological Society, Inc.; delegate to the American Medical Association and Chairman of the Section of Ear, Nose and Throat; he was a member of the American Otological Society, Inc.; and a member of the Board of Governors of the American College of Surgeons.

Dr. Shurly's local clubs included the Army and Navy, Country, Detroit, Grosse Pointe, Prismatic and University.

Following his death October 20, 1950, due to coronary occlusion, Dr. Shurly received many tributes from his fellow townsmen:

"He was beloved of all who sat with him in the civic, educational and other bodies which attracted his gregarious nature and enlisted his purposeful concern." (Det. News, 10-21-50)

"In death Dr. Shurly continues to live in the hearts of the hundreds of thousands who have benefitted from his many years of public service." (Det. Bd. of Educ., Vol. 11, No. 3)

"All of us will miss Burt, fellow-physician and friend." (Dr. William J. Stapleton, Det. Med. News, 11-6-50)

Dr. Shurly is survived by his wife, Viola Palms Shurly; two sons, Burt, Jr., and Edmund R.; three daughters, Mrs. Storm Vanderzee, Mrs. Beatrice Wilcox and Mrs. Clarkson Wormer III; and thirteen grandchildren.

J. M. S.

Abstracts of Current Articles

EYE

The Various Movements of the Human Eye on Rotation about Different Axes.

Jongkus, L. B. W., and Hulk, J.: Acta Oto-Laryngologica 38:274 (June) 1950.

Using a turning room the authors have tried to verify Flourens' law, that stimulation of a semicircular canal resulted in a particular type of nystagmus. They were able to prove that stimulation of a semicircular canal causes movements in the direction of that canal but not, as has been frequently misquoted, that each canal causes a nystagmus in its own plane. The form of nystagmus depends not only upon the axis of rotation in relation to the position of the body but also in the direction of gaze. Examination in the planes of the canals is the preferable procedure.

HILL.

EAR

On the Extirpation of the Malleus from the Tympanic Membrane.

Miodoyski, J.: Acta Oto-Laryngologica 38:250 (June) 1950.

The author found it very easy to remove the entire malleus from the tympanic membrane in two cases of chronic middle ear suppuration. Later he followed this procedure in doing a fenestration, finding it more difficult, though completely successful. This allowed the formation of a completely flexible plastic flap to cover the fenestra.

HILL.

NOSE

Rhinolith as a Cause of Suppurative Rhinitis.

Nochlas, N. E.: New England J. of Med. pp. 244-1 (Jan. 4) 1951).

A case of rhinolith complicated by rhinitis caseosa is reported. This measured 2 by 1.5 cm and had completely destroyed the lateral nasal wall and perforated the septum. No cholesterol crystals were found. The author, quotes Kelemen who cites Render as attributing osteogenic properties to sinus mucous membranes, and states that histopathological examination of the involved mucous membrane

showed areas of new bone formation. He suggest that these areas later might have formed the nucleus of new rhinoliths.

HILL.

LARYNX

The Respiratory Function in Laryngectomized Patients.

Heyden, R.: Acta Oto-Laryngologica Suppl. 85.

This work is based upon careful spirometric determinations of lung volume and studies of respiration with work tests, using the bicycle ergometer, as well as the incidence of respiratory infections, state of general health and social adaptation of 44 laryngectomy patients. Fitness to perform physical work was found in 67 percent of this series. No increased susceptibility to respiratory infection was noted. Most of the cases exhibited a somewhat low pulmonary vital capacity, but the respiratory response to work tests was normal in most of the cases investigated. Thirty percent of the group were 65 years of age or older, and consequently would not be expected to be able to perform hard physical labor. Respiratory insufficiency with work did not occur any more frequently in this group than in a control group of corresponding age distribution. No definite changes as a consequence of the operation could be demonstrated. While only 55% developed esophageal speech, 88% had serviceable speech such as to enable them to be understood on the telephone.

HILL.

ESOPHAGUS

Corrosion of the Esophagus and Diseases of the Lungs, Especially Pulmonary Tuberculosis.

Kiviranta, V. K.: Acta Oto-Laryngologica 38:353 (Aug.) 1950.

380 cases of lye stricture of the esophagus were studied in an effort to ascertain the frequency of subsequent development of pulmonary tuberculosis. It was found that inflammatory diseases of the thoracic structures were common. These included esophagitis, periesophagitis, diverticula, esophago-tracheal fistulae, mediastinitis, mediastinal abscesses, pleurisy, empyemata, pericarditis and pneumonia. Oftentimes these conditions presented changes which might be interpreted as tuberculosis. Eight of these cases developed esophageal carcinoma. True tuberculosis was found only in one of the 380.

HILL.

MISCELLANEOUS

Non-epidemic Parotitis in a Series Collected from an Otorhinolaryngological Clinic.

Adner, C. A.: Acta Oto-Laryngologica 38:333 (Aug.) 1950.

In a study of 24 cases of non-epidemic parotitis the author states that most infections of the parotid are due to ductogenic infections, with poor oral hygiene, atrophic mucosa, poor general health and other infectious diseases as predisposing causes. Calculi rarely are the cause of infection in the parotid, although foreign bodies in the duct may result in swelling of the gland. The role of dehydration is well-recognized. Many cases are allergic in origin. The sparsity of bacteria-inhibiting mucin in the secretion of the parotid makes it the most frequently infected of the salivary glands. Xerostomia is frequently a factor in parotitis.

HILL.

Recurring Meningitis.

Merek, L.: Acta Oto-Laryngologica 38:201 (June) 1950.

The greatest danger of a secondary meningitis is due to the fact that it may be considered a primary infection. Adequate therapy may result in disappearance of symptoms, to be followed by recurrence unless the latent focus is eradicated. New foci may develop during the course of the disease. Study of the cisternal, as well as the spinal fluid may give valuable information due to the possibility of spinal blockade. Foci may be otogenic or rhinogenic.

HILL.

The Early Treatment of Common Colds with an Antihistaminic: Histadyl.

Browning, R. H.: New England J .of Med. pp. 243-45 (Dec. 21) 1950.

As a result of a controlled study of 617 college students no evidence was presented that Histadyl (thenylpyriline hydrochloride) had any effect in aborting or ameliorating colds. The students were divided into three groups. Group A received histadyl; Group B a placebo; while Group C abstained from any medication. The students in Group B receiving the placebo showed the lowest percentage of colds indicating the important psychologic effect of taking medication whether placebo, or other.

HILL.

Tonsillectomy as Treatment of Acute Peritonsillitis, with Clinical and Statistical Observations.

Virtanen, V. S.: Acta-Laryngologica Suppl. 80.

An exhaustive study of 379 cases of peritonsillar abscess treated by tonsillectomy. The series included 15 cases of parapharyngeal space abscess. Thirteen of these were cured by tonsillectomy followed by incision through the tonsillar fossa. In only two cases was external drainage required. Three hundred and sixty-four or 96% were considered as cases of "uncomplicated peritonsillitis." Postoperative hemorrhage occurred as a complication in only six cases. Six other cases had pulmonary complications of pneumonia or bronchitis probably due to aspiration. These were reported as of brief duration. One patient, the only fatality, in this group, was found to have well-advanced tuberculosis and died two weeks after operation. Fifteen, or 4%, were considered as "complicated peritonsillitis" due to sepsis, parotitis, cervical lymph-adenitis, or deep neck infection. Five of the septic patients died. The author concludes the abscess tonsillectomy is a serviceable therapeutic procedure which does not involve any greater risks than other surgical measures. Some twenty years ago this procedure was advocated by certain laryngologists in this country although it never had wide acceptance. With modern antibiotic and chemotherapeutic methods it seems doubtful if there would be much justification for employing this today, except in the so-called "blind abscess." In cases of deep neck infection external operation plus antibiotic therapy would seem advisable, delaying the removal of the tonsils until all acute manifestations have subsided.

HILL.

Books Received

Nasal Sinuses.

By O. E. Van Alyea, M. D., Associate Clinical Professor, Department of Laryngology, Rhinology and Otology, University of Illinois College of Medicine, Chicago. Pp. xv+327, with 143 illustrations, 15 in color. Baltimore, Maryland, The Williams & Wilkins Company, 1951. (Price $9.00)

Allergie et Troubles vasomoteurs de la Muqueuse nasale et sinusienne.

By R. Melchior. Pp. 160. Paris, Masson et Cie, 1950. (Price 650 fr.)

Current Therapy 1951. Latest Approved Methods of Treatment for the Practicing Physician.

Editor: Howard F. Conn, M.D. Consulting Editors: M. Edward Davis, Vincent J. Derbes, Garfield G. Duncan, Hugh J. Jewett, William J. Kerr, Perrin H. Long, H. Houston Merritt, Paul A. O'Leary, Walter L. Palmer, Hobart A. Reimann, Cyrus C. Sturgis, Robert H. Williams. Pp. xxxi+699. Philadelphia and London, W. B. Saunders Company, 1951. (Price $10.00)

Notices

UNIVERSITY OF ILLINOIS INITIATES MODIFIED PROGRAM

For the period of the National Emergency, the University of Illinois College of Medicine will offer a combined three year residency training program in Otolaryngology, which will include the basic course material, in fulfillment of Board requirements.

Residents will rotate through the Research and Educational Hospitals, the Illinois Eye and Ear Infirmary, the Hines Veterans Administration Hospital and the various affiliated institutions. The residency will be so flexible that should it be interrupted because of military service, the period of training may be resumed upon returning to civilian life.

Under this arrangement, no course fee is to be involved and in the case of most of the aforementioned institutions, a stipend is provided.

For further information, kindly address; Head of the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

NOTICE

The American Board of Otolaryngology will conduct the following examinations in 1951:

May 1-4, in Richmond, Virginia, at the Hotel John Marshall.

October 9-12, in Chicago, Illinois, at the Palmer House.

DEAN M. LIERLE, M.D., *Secretary*
University Hospital,
Iowa City, Iowa

HOME STUDY COURSES

The 1951-1952 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of ten months. Registrations must be completed before August 15. Detailed information and application forms may be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 100 First Avenue Building, Rochester, Minnesota.

THIRD PAN-AMERICAN CONGRESS

The Pan American Association of Oto-Rhino-Laryngology and Broncho-Esophagology will hold its Third Pan American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology in Havana, Cuba, in 1952.

For information address: Dr. Chevalier L. Jackson, 3401 N. Broad Street, Philadelphia 40, Pa.

SECOND LATIN-AMERICAN CONGRESS

The Second Latin American Congress of Otorhinolaryngology and Bronchoesophagology will meet in Sao Paulo, Brazil, in July, 1951.

President: Professor A. de Paula Santos.

Secretaries: Dr. Jose de Rezende Barbosa, Dr. Plinio de Mattos Barretto, Hospital das Clinicas, Sao Paulo, Brazil.

NOTICE

The management of the ANNALS desires to buy, at $1.50 each, copies of the following numbers which are out of print:

March, June, 1940	March, Dec., 1946
March, June, 1943	June, Sept., 1947
March, Sept., Dec., 1944	March, Dec., 1948
March, June, Sept., Dec., 1945	March, 1950

HEARING AIDS ACCEPTED BY THE COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION THE AMERICAN MEDICAL ASSOCIATION

(List Corrected to March 1, 1951)

Aurex Model F
Aurex Model H

Beltone Harmony Mono-Pac
Beltone Symphonette
Beltone Mono-Pac Model M

Cleartone Model 500
Cleartone Regency Model

Dysonic Model No. 1

Electroear Model C

Gem Model V-35
Gem Model V-60

Maico Atomeer
Maico UE Atomeer
Maico Quiet Ear Models G & H
Mears Aurophone Model 200
1947-Mears Aurophone Model 98
Micronic Model 101 (Magnetic Receiver)
Micronic Model 303 (See Silver Micronic)
Microtone T-3 Audiomatic
Microtone T-5 Audiomatic
Microtone Classic Model T9
Microtone Classic Model 45

National Cub Model (C)
National Standard Model (T)
National Star Model (S)
National Ultrathin Model 504
National Vanity Model 506

Otarion, Model E-1S
Otarion, Model E-2
Otarion, Model E-4
Otarion Models F-1, F-2 and F-3

Paravox Models VH & VL (Standard)
Paravox Model XT ('Xtra-Thin)
Paravox Model XTS ('Xtra-Thin)
Paravox Model Y (YM, YC and YC-7 (Veri-small)

Radioear Permo-Magnetic Multipower
Radioear Permo-Magnetic Uniphone
Radioear All-magnetic Model 55
Radioear Model 62 Starlet

Silver Micronic (Magnetic and Crystal) Models 202M & 202C (See Micronic)
Silvertone Model 103BM
Silvertone Model M-35
Silvertone Model P-15
Solo-Pak Model 99
Sonotone Model 600
Sonotone Model 700
Sonotone Model 900
Sonotone Models 910 & 920
Sonotone Model 925
Super-Fonic Hearing Aid

Televox Model E
Telex Model 22
Telex Model 97
Telex Model 99
Telex Model 200
Telex Model 1700
Tonemaster Model Royal
Trimm Vacuum Tube Model 300

Unex Model A
Unex Midget Model 95
Unex Midget Model 110

Vacolite Model J

Western Electric Model 63
Western Electric Model 64
Western Electric Models 65 & 66

Zenith Model 75
Zenith Miniature 75

(All of the accepted hearing devices employ vacuum tubes.)

Accepted hearing aids more than five years old have been omitted from this list for brevity.

TABLE HEARING AIDS

Aurex (Semi-Portable)
Precision Table Hearing Aid
Sonotone Professional Table Set Model 50